CATALYSIS IN CHEMICAL
AND PETROCHEMICAL INDUSTRY

Methods for the Catalytic Synthesis of Piperazine

E. E. Sergeev[a,]*, L. L. Gogin[a], T. B. Khlebnikova[a], E. G. Zhizhina[a], and Z. P. Pai[a]

[a] *Boreskov Institute of Catalysis, Siberian Branch, Russian Academy of Sciences, Novosibirsk, 630090 Russia*
***e-mail: evges@catalysis.ru**

Abstract—Piperazine synthesis methods on intermolecular and intramolecular cyclization catalytic processes are compared and reviewed analytically. The advantages and disadvantages of current ways of synthesizing piperazine are described while focusing on the preferred and highly selective processes of intramolecular cyclization using aminoethylethanolamine and diethylenetriamine, and one-step intermolecular cyclization using ethylenediamine, mono-, and diethanolamine.

INTRODUCTION

Piperazine (PP) or 1,4-diazacyclohexane is the simplest cyclic ethyleneamine homolog. It is a valuable product used in the production of surfactants, antioxidants, plastics, synthetic resins and fibers, rubbers, corrosion inhibitors, and catalysts for preparing polyurethanes, dyes, and effective pharmaceuticals (piperazine is used as a strong anthelmintic in particular) [1].

A report provided by Cognitive Market Research (United States) indicates that PP production is currently 51.5 thousand tons per year, and its consumption will increase by 3−4% annually according to forecasts [2]. The following foreign companies make a major contribution to the world production of PP: The Dow Chemical Company and Huntsman Corporation (United States), BASF SE (Germany), Akzo Nobel NV (Netherlands), Delamine BV (Netherlands), Tosoh Corporation (Japan), Nippon Nyukazai (Japan), Diamines & Chemical Limited (India), Hebei Hejia Pharmaceutical Group (China), and Shaoxing Xingxin New Materials Corp. Ltd (China). PP is a by-product of producing ethylenediamine (EDA) from dichloroethane (DCE) and ammonia or monoethanolamine (MEA) and ammonia [3, 4]. At the same time, half of its global consumption is in the Asia−Pacific region (China, Japan, India, and Southeast Asia), followed by North America, the European Union, Central and South America, the Middle East, and Africa.

PP is not produced in Russia. The need for PP is fully met by imports, and the domestic market is monopolized by European and Chinese suppliers. The average price is within $8000 per ton. The imported product is purified after purchase, if necessary.

An important task for Russia under the conditions of sanctions from the Western countries, the insufficient purity of the product of Asian manufacturers, and the import substitution program is to organize the small-scale production of PP using readily available and cheap domestic raw materials. The technologies underlying them must also meet modern environmental requirements.

All catalytic ways of obtaining the target product (PP) can therefore be conditionally divided into two groups to analyze the literature and patents: processes based on intermolecular or intramolecular cyclization, depending on the raw materials that are used [5]. Intramolecular reactions are another way of preparing PP through its hydrogenation.

1. CATALYTIC PIPERAZINE PRODUCTION METHODS BASED ON INTERMOLECULAR CYCLIZATION

1.1. Preparing PP by EDA Cyclization with DCE

PP is a by-product of the industrial synthesis of EDA, which is obtained by DCE ammonolysis [6] and the catalytic amination of MEA [7]. The maximum amounts of PP in the reaction product during this process are, however, 1.9 and 9.2%, respectively [3, 4]. Ways of improving these processes to synthesize PP are therefore described in the literature.

The first stage of the reaction between EDA and DCE is the formation of 2-chloroethylethylenediamine hydrochloride, which undergoes intramolecular cyclization in alkaline solutions at 20−50°C to transform into PP (Fig. 1) [8, 9].

EDA and DCE are mixed in 1,2-dichlorobenzene in an 8 : 1 molar ratio inside a reactor equipped with a

$$H_2N \diagdown NH_2 + Cl \diagdown Cl \longrightarrow Cl \diagdown NH \diagdown NH_2 \cdot HCl \xrightarrow[-2HCl]{OH^-} HN \diagup \diagdown NH$$

EDA   DCE   PP

Fig. 1. Scheme of PP synthesis by EDA cyclization with DCE.

reflux condenser. The reaction is conducted at 20°C for 24 h. DCE conversion is 98%, and the yield of PP is 67% [10]. Many linear and branched ethyleneamines form if DCE reacts with ammonia water, and the selectivity toward PP is low. It should be noted that some PP can appear in the products of ethyleneimine polymerization in liquid NH_3 when using NH_4Cl [11]. It is very difficult to isolate PP from polymer in this process, so this technique is generally not used.

A disadvantage of this approach is low selectivity toward PP because of the formation of linear and branched ethyleneamines. DCE is also a carcinogen, and the hydrochloride that is released corrodes equipment. DCE does not meet the requirements of medicinal products, since it contains chlorine impurities. Selective processes would therefore seem to be promising for pharmacological purposes in order to produce PP using ethanolamines as raw materials.

1.2. Preparing PP by MEA Cyclocondensation

PP is prepared by MEA cyclocondensation (with and without ammonia) continuously or in batches. Figure 2 shows the scheme of synthesis.

The condensation of MEA (1 mol) inside a shaken autoclave with Raney Ni catalyst (8.2 wt %) in 1,4-dioxane for 5 h at 190–200°C and a H_2 pressure of 2.0–2.7 MPa was described in [12]. Hydrogen was required to maintain the activity of the catalyst and suppress side dehydrogenation reactions that result in the formation of pyrazine and pyrrolidine. The yield of the target product (PP) was 24.2% (Table 1, entry 1). The authors showed that MEA undergoes strong thermolysis with no solvent, and the yield falls to 12.1% (Table 1, entry 2).

The reaction between MEA and ammonia is used in industry to obtain EDA [3, 4]. The reaction conditions are 150–230°C, 20 MPa, and Ni-based catalyst with additions of Cu, Co, Cr, Fe, Ru, B or Cu–Co. As was noted above, this results in a mixture of products containing up to 9.2% PP. The product is separated via fractional distillation.

$$2H_2N \diagdown OH \xrightarrow[-H_2O]{Cat} HN \diagup \diagdown NH$$

MEA   PP

Fig. 2. Scheme of PP synthesis by MEA cyclocondensation.

PP is also obtained by converting MEA in mixtures with NH_3 [13]. Gaseous NH_3 and MEA are passed into a flow reactor heated to a temperature of 280–300°C over 5% ThO_2/Al_2O_3 catalyst at atmospheric pressure. The period of contact is 10–30 s, while that of catalyst operation is 2–5 h. The conversion of MEA is 70–80% complete. PP, the yield of which is 37%, is isolated via fractional distillation from the resulting mixture of amines (Table 1, entry 3).

PP can be obtained as the main product via the condensation of MEA hydrochloride or hydrobromide at 240–250°C. The reaction proceeds until the resulting water is no longer distilled off. The yields of PP are 44 and 51%, respectively. If MEA reacts with NH_4Cl in equimolar amounts under the same conditions, the yield of PP falls to 30% [14].

Higher yields of the target product (up to 45%) are reached when MEA is condensed with NH_3 inside a rotation autoclave for 4 h at a H_2 pressure of 0.7 MPa with Raney Ni (9.5 wt %) at 200°C (Table 1, entry 4) [15].

The condensation of MEA (1 mol) in liquefied NH_3 (2.5 mol) at a H_2 pressure of 9 MPa using catalysts was described as an example in [16, 17]. Studies were performed using a rotation autoclave and catalysts Ni–Al alloy, Ni, and Co metals supported on pumice, kieselguhr, SiO_2, Al_2O_3–SiO_2, different Al_2O_3, ZrO_2, TiO_2, ZnO, MgO, and $Ca_3(PO_4)_2$. Out of many metal oxide additives, only MgO and BaO raised the rate of the reaction slightly. The yield of the target product grew by 0.5 wt %, and the effect of MgO was stronger with a 20% $Co/\alpha-Al_2O_3$ catalyst (PP yield, 49.8%). By studying the conditions of the reaction, it was established that the optimum temperature was 200°C, the H_2 pressure was 9–12 MPa, and the amount of 20% $Co/\gamma-Al_2O_3$ catalyst was 10–15 wt % of the weight of MEA. The yield of PP was as high as 55–60% under these conditions (Table 1, entry 5). The products of hydrogenolysis were mainly identified without NH_3, and PP was detected only in trace amounts. NH_3 and H_2 prevent deamination, and thus increase the yield of PP.

PP can be synthesized catalytically via the amination of MEA without H_2 [18]. A gas–liquid mixture with a NH_3 : MEA molar ratio of 5.63 at a pressure of 0.9 MPa is fed into a flow tube reactor heated to a temperature of 256°C with 65–78% NiO, 15–25% CuO, and 1–10% $Cr_2O_3/\gamma-Al_2O_3$ (plus small amounts of Co and W) as catalysts. The selectivity toward PP is 54%, and its yield is 25% (Table 1, entry 6). Products of

Table 1. Ways of obtaining PP based on intermolecular cyclization

No.	Components (ratios)	Catalyst (wt %)	H_2 pressure, MPa	T, °C	Reaction time, h	Yield of PP, %	Side products, (solvent)	Ref.
1	2	3	4	5	6	7	8	9
	(a) Catalytic cyclocondensation of MEA in continuous and batch process							
1[1]	MEA	Raney Ni (8%)	2.0–2.7	190–200	5	24.2	(1,4-Dioxane)	[12]
2[1]	MEA	5%ThO_2/Al_2O_3	—	280–300	2–5	12.2	Oil liquid	[13]
3	MEA/NH_3	Raney Ni (9.5%)	0.7	200	4	37	Me_3N, Et_3N etc.	[15]
4	MEA/NH_3	20%Co/γ-Al_2O_3	9–12	200	3–6	45	EDA, AEEA, DETA etc.	[16]
5[1]	MEA/NH_3(1/2.5–3)	NiO-CuO-Cr_2O_3/γ-Al_2O_3	—	256	—	55–60	—	[18]
6[1,2]	NH_3/MEA(5.63/1)	Ni-Cu/SiO_2	0.4–0.6	200–220	3	25	—	[20]
7[3]	MEA					38.7–47.8		
8	MEA/NH_3/H_2O	20%Co/H-ZSM-5	6	230	—	35	EDA, AEEA, DETA etc.	[21]
9	NH_3/MEA(0.7/1)	KCl-NiO-ZSM-5	—	360	—	20.1	4.2% TEDA	[22]
	(b) Catalytic cyclocondensation of EDA with EG in batch mode							
10	EDA + EG(1/1)	Raney Ni (6.6%)	2.0–2.7	190–200	5	24.2	(1,4-Dioxane)	[12]
11[4]	EDA + EG(2.4/1)	Raney Cu (up to 20%)	11.8	210	6	70	(Simple ethers)	[23]
12	EDA + EG(1/1)	0.8%Pd/MgO	—	160	6.5	80	MeCN	[24]
13	EDA + EG(1/1)	$Ru_3(CO)_{12}$–PBu_3 (0.48/1.4% mol.)	—	220	15–18	100	(THF)	[25]
					5	88	(1,4-Dioxane)	
	(c) Catalytic cyclocondensation of EG with NH_3							
14[1]	EG/NH_3(1/2)	Cu-Ni-Cr (16%)	20.4	242–248	2	31	—	[26]
15	NH_3/EG/H_2(30/1/1)	Ni-Cu/ mordenite	10	230	—	31.5	—	[27]
	(d) Catalytic cyclodeamination of EDA							
16	EDA/H_2O(1/12)	KZSM-5	—	340	72	48	PR, 2-picoline, resins	[28]
17	50% EDA/H_2O	HZSM-5-KZSM-5 (2.6%)	—	340	—	91.7	TEDA	[29]
18	40% EDA/H_2O	$CaCl_2$–HZSM-5	—	340	—	65	25% TEDA	[30]
19	EDA/H_2O(4/6)	Zn-ZSM-5	—	360	—	42.8	27.7% TEDA	[31]
20	EDA/H_2O(4/6)	Zn/K-ZSM-5	—	360	—	34.8	41.4% TEDA	
21	EDA/H_2O(0.9/1)	SO_4^{2-}/ZrO_2	—	260	—	85	—	[32]
	(e) Catalytic cyclodehydration amination of DEA							
22[1]	DEA·HCl/NH_4Cl(1/1)	Raney Ni (21.4%)	7	200	4	33	1-Et and 1,4-Et_2PP, MOR, EtOH, and $EtNH_2$	[34]
23	DEA/NH_3/H_2(1/10/33.6)	Fe_3O_4–V_2O_5 or Cr_2O_3 (2–5)	3.7	230	—	61	—	[35]
24	80% DEA–H_2O/NH_3(1/13)	Ni,Co,Cu,Sn/Al_2O_3	19–20	190	—	62.1	EDA, DETA, and AEEA	[36]

(1) Reactor was an autoclave.
(2) Co and W additives.
(3) $H_3PW_{12}O_{40}$ additive (0.2–0.5 wt %).
(4) Dehydration agents were (5–30 wt %) Na_2SO_4 or $MgSO_4$.

$$H_2N \diagdown NH_2 + HO \diagdown OH \xrightarrow[-2H_2O]{Cat} HN \hexagon NH$$

EDA EG PP

Fig. 3. Scheme of PP synthesis by catalytic EDA cyclocondensation with EG.

MEA amination always contain EDA, the amount of which can be reduced by introducing H_2. The EDA : PP ratio of the products is inversely proportional to the rate of H_2 supply at a constant conversion of MEA [19].

PP can be synthesized using a gas-phase approach without NH_3 [20]. MEA is condensed at H_2 pressures of 0.4–0.6 MPa and temperatures of 200–220°C inside a tubular reactor on catalyst of (40–50%) Ni and (10–15%) Cu/SiO$_2$ with additions of Keggin phosphotungstic heteropoly acid $H_3PW_{12}O_{40}$ in amounts of 0.2 to 0.5 wt. %. The conversion of MEA is 65–78%, and the PP selectivity is 59.6–61.3% with yield of 38.7–47.8% (Table 1, entry 7) [20]. The catalytic activity falls over time, and the amount of heteropoly acid is reduced, due to the formation of solvates with nitrogen-containing reaction products. The catalyst is therefore gradually deactivated after 3 h.

A procedure based on MEA amination in a flow tubular reactor with a 20% Co/H-ZSM-5 catalyst was proposed in [21]. A 40% aqueous solution of MEA with NH_3 was fed into the reactor at a temperature of 230°C and a H_2 pressure of 6 MPa. The conversion of MEA was 76.8%, the PP selectivity was 45.7%, and the yield of PP was 35% (Table 1, entry 8).

There is also a way of PP synthesis by catalytic MEA condensation with NH_3 at normal pressure in a flow tubular reactor, based on ZSM-5 zeolite modified with KCl, NiO, and ZnO. KCl-NiO-ZSM-5 catalyst displayed high activity in this process at a temperature of 360°C with a NH_3 : MEA molar ratio of 0.7. The conversion of MEA was 66.8%. The selectivity and yield of PP were 30.2 and 20.1%, respectively, while those of triethylenediamine (TEDA) were 6.3 and 4.2%, respectively (Table 1, entry 9) [22].

Periodical processes that can be recommended for the organization of small-scale production of PP thus have higher yields of PP (45 and 55–60%) than any other catalytic methods of MEA cyclocondensation (Table 1). A continuous process with stable catalyst operation provides a low product yield of 35%, but it has the advantage of productivity and can be considered for the medium and high-tonnage production of PP using readily available and cheap raw materials.

1.3. Preparing PP by EDA Cyclocondensation with Ethylene Glycol

Many procedures for obtaining PP by catalytic EDA cyclocondensation with EG are performed in a periodic way (the scheme of synthesis is shown in Fig. 3).

The target product can be obtained via the catalytic cyclocondensation of EDA with EG in equimolar amounts (0.5 mol each) in 1,4-dioxane solutions (0.75 mol) using Raney Ni (6.6 wt %) under conditions similar to MEA condensation [12]. The yield of PP in this process is low at 24.2% (Table 1, entry 10).

Good results were obtained using the autoclave condensation of EDA (1.16 mol) and EG (0.48 mol) with Raney Cu catalyst (up to 20 wt %) and anhydrous Na_2SO_4 (5–30 wt %) as the dehydration agent [23]. The process was conducted in a H_2 atmosphere at a pressure of 11.8 MPa and temperatures around 210°C. The yield of PP was 70% after 6 h (Table 1, entry 11).

Very good results were obtained when the reaction between EDA and EG in equimolar amounts (12 mmol each) was conducted inside an autoclave for 6.5 h using a MeCN solution (19 mmol) containing Pd/MgO (7.5 μmol) at a temperature of 160°C in an inert atmosphere. The conversion of EDA was 94%, and the yield of PP was 80% (Table 1, entry 12) [24].

The best results were obtained for the condensation of equimolar amounts of EDA with EG (27 mmol each) in tetrahydrofuran solution (24.7 mmol) containing $Ru_3(CO)_{12}$-PBu$_3$ catalytic complex (0.13/0.39 mmol) at 220°C and normal pressure over 15–18 h. The yield of PP was close to 100%. When tetrahydrofuran was replaced with 1,4-dioxane (23.4 mmol), the yield of PP fell to 88% after 5 h of the reaction [25]. The disadvantages of a homogeneous catalytic reaction are the step of separating the catalyst from reaction products and its high cost.

Table 1 (subgroup b) summarizes the data on producing PP via the catalytic cyclocondensation of EDA with EG. The table shows that the highest yields of PP—80 and 100 (88%) (entries 12 and 13)—are observed for processes in which aprotic solvents, homogeneous $Ru_3(CO)_{12}$-PBu$_3$, and 0.8% Pd/MgO heterogeneous catalysts containing precious metals were used. This way of synthesizing PP combined with available and cheap raw materials can be recommended as the one most promising for its small-scale production.

Fig. 4. Scheme of PP synthesis by catalytic EG condensation with NH_3.

Fig. 5. Scheme of PP synthesis by catalytic EDA cyclodeamination.

1.4. Preparing PP by EG Cyclocondensation with NH_3

PP can be prepared by catalytic EG cyclocondensation with NH_3 by periodic and continuous means. The scheme of synthesis is shown in Figure 4.

PP can be obtained in an autoclave via the interaction between EG (2 mol) and precondensed NH_3 (4 mol) on a Cu–Ni–Cr catalyst (16 wt %) in a H_2 atmosphere with a total pressure of 20.4 MPa at temperatures of 242−248°C. The reaction lasts 2 h, and the yield of PP is 31% [26]. It should be noted that PP does not form in the gas phase, due to the thermolysis of EG.

The continuous catalytic synthesis of PP was conducted via the hydroamination of EG on a bimetallic Ni–Cu composition using mordenite zeolite as a support [27]. A flow of components with a molar ratio of $NH_3 : EG : H_2 = 30 : 1 : 1$ was fed into a flow tubular reactor heated to 230°C at a pressure of 10 MPa with a rate of $0.2\ h^{-1}$. The conversion of EG was 42%, and the selectivity and yield of PP were 75 and 31.5%, respectively. A comparison of these two techniques (Table 1, entries 14 and 15) indicates they have similar yields of ≈31%, but the continuous process has better performance.

1.5. Preparing PP by Catalytic EDA Cyclodeamination

Many ways of obtaining PP by catalytic EDA cyclodeamination are continuous, according to the scheme presented below.

PP can be synthesized via the catalytic intermolecular cyclodeamination of EDA with steam [28]. The reaction is conducted inside a tubular flow reactor on ZSM-5 type zeolites modified with alkali metals. Of the considered catalysts, KZSM-5 showed the best results at a temperature of 340°C and an $EDA : H_2O$ molar ratio of 1 : 12 . The conversion of EDA fell from 90 to 80% within 72 h, while the selectivity of PP rose from 50 to 60% and its yield grew from 45 to 48% (Table 1, entry 16).

Subsequent studies in this area were aimed at modifying zeolite catalysts. PP was synthesized continuously via the vapor–gas phase intermolecular cyclodeamination of a 50% aqueous solution of EDA on H-ZSM-5 catalyst with 2.6 wt % K-ZSM-5 at 340°C and a volumetric feed rate of raw materials of $2.3\ h^{-1}$ [29]. The conversion of EDA was 95.3%, and the selectivity and yield of PP were 96.2 and 91.7%, respectively (Table 1, entry 17).

The authors deaminated a 40% EDA aqueous solution in the flow mode on $CaCl_2$-HZSM-5 catalyst at 340°C and a reagent flow rate of 0.4 mL/min [30]. The conversion of EDA was more than 95%, the yield of PP was 65%, and the yield of the TEDA by-product was 25%.

PP can also be synthesized continuously via the deamination of an aqueous solution with an $EDA : H_2O = 4 : 6$ molar ratio on Zn-ZSM-5 and Zn/K-ZSM-5 catalysts at 360°C with a feed space velocity of 0.25 g/(min h) [31]. The conversion of EDA was 94.1 and 82.6% for these catalysts, while the selectivity and yield of PP were 45.5 and 42.1%, and 42.8 and 34.8, respectively. It should be noted that introducing more Zn increased the yield of undesirable product (TEDA), which was 27.7 and 41.4% at comparable values of conversion on H-ZSM-5 and K-ZSM-5 catalysts, respectively (Table 1, entries 19 and 20).

Another version of this process was described in [32]. PP was produced via the continuous vapor–gas phase deamination of EDA aqueous solution with an $EDA : H_2O = 0.9{:}1$ molar ratio on a SO_4^{2-}/ZrO_2 solid superacid catalyst at 260°C in an atmosphere of N_2. The feed space velocity was 0.12 mL/min. The yield of PP was 85% and lower than 5% without water. The authors noted that an advantage of this process is the high rate of the reaction, and the catalyst displayed high activity and chemical stability. High temperatures also promote the intramolecular dehydrogenation of PP to PR.

An analysis of ways of obtaining PP via the catalytic cyclodeamination of EDA indicates that SO_4^{2-}/ZrO_2 superacid catalyst and HZSM-5-KZSM-5 zeolite-based catalytic systems, which allow us to achieve high yields of PP (85 and 91.7%), seem to be best for effective vapor–gas phase processes. The process in which a solid superacid catalyst is used is conducted at a lower temperature and a faster rate. Advantages of this process are low risk of fire and explosion at atmospheric pressure.

1.6. Preparing PP by the Cyclodehydration Amination of Diethanolamine

PP can be obtained via the catalytic cyclodehydration amination of DEA using periodic and continuous means (Fig. 6).

PP can be obtained as the main product of heating pure DEA hydrochloride at 250−260°C until the water

$$HO \diagdown \diagup NH \diagdown \diagup OH + NH_3 \xrightarrow[-2H_2O]{Cat} HN \diagup \diagdown NH$$

DEA   PP
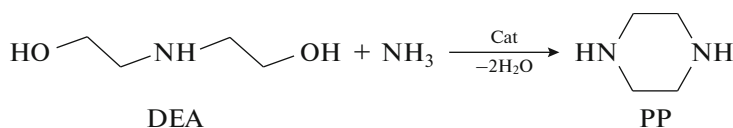
Fig. 6. Scheme of PP synthesis via the catalytic cyclodehydration amination.

formed from condensation ceases to be distilled off. Its yield is low at 8−10%, but if the reaction between DEA hydrochloride and NH_4Cl proceeds under the same conditions at molar ratios of 1 : 1 and 1 : 2, the yield of PP grows to 23.0 and 26.7%, respectively [33].

Higher yields can be reached if the reaction proceeds in an autoclave by heating a mixture of DEA hydrochloride and NH_4Cl taken in equimolar amounts (2 mol each). The reaction is conducted for 4 h at a H_2 pressure of 7 MPa using Ni- Raney catalyst (21.4 wt %) at 200°C, and the yield of PP is 33% [34].

Good results are obtained when the catalytic hydroamination of DEA is conducted on reduced crushed Fe_3O_4 alloy (2−5 wt %) with V_2O_5 or Cr_2O_3 as promoters [35]. A mixture with a partial pressure of DEA of 0.11 MPa, NH_3 of 1.1 MPa, and H_2 of 3.7 MPa and a volumetric feed rate of V_{DEA} of 220 g/(h L_{kat}) is fed into a flow tubular reactor heated to a temperature of 230°C. The conversion of DEA is 91%, and the selectivity and yield of PP are 67 and 61%, respectively.

The best results are obtained for the reductive amination of 80% DEA aqueous solution on a catalytic system of (12−20%) Ni, (12−20%) Co, (4−12%) Cu, and (0.6−2.2)Sn/Al_2O_3 [36]. A DEA/NH_3 liquid mixture with a molar ratio of 1 : 13 in a H_2 atmosphere and a total pressure of 19−20 MPa is fed from below into a flow-through vertical tubular reactor heated to a temperature of 190°C. The conversion for DEA is more than 90%, and the selectivity and yield for PP are 69 and 62.1%, respectively (Table 1, entry 24).

There have been a number of studies in which small amounts of PP were obtained via the thermolysis of triethanolamine through the stage of MOR formation, along with the processes of this group [37]. This process is, however, of no practical importance. The same negligible amount of PP forms during the catalytic interaction between NH_3 and ethylene oxide, where mostly mono-, di-, and triethanolamines are obtained.

$$H_2N \diagdown \diagup NH \diagdown \diagup OH \xrightarrow[-H_2O]{Cat} HN \diagup \diagdown NH$$

AEEA   PP
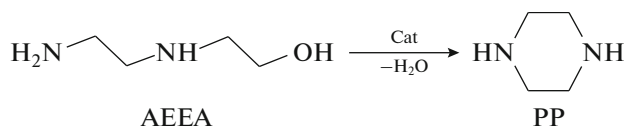
Fig. 7. Scheme of PP synthesis by catalytic AEEA cyclodehydration.

2. CATALYTIC PIPERAZINE PRODUCTION METHODS BASED ON INTRAMOLECULAR CYCLIZATION

2.1. Preparing PP by AEEA Cyclodehydration

Processes for obtaining PP by catalytic AEEA cyclodehydration are conducted in periodic and continuous ways. The scheme of synthesis is shown in Figure 7.

Catalytic AEEA cyclodehydration was initially developed using homogeneous catalysts and then such massive catalysts as Cu- or Raney Ni.

A way of synthesizing PP as a hydrochloride with a yield of 79% was described [38]. The target product was obtained by AEEA dehydrocyclization on a [Cp·IrCl_2]_2 catalytic complex (0.25 wt %) in a $NaHCO_3$ aqueous solution (2 wt. %) at 140°C over 48 h (Table 2, entry 1).

AEEA (245°C) was boiled for several hours in a reaction vessel along with phosphorus-containing catalysts ($NaPO_3$, H_3PO_4, $POCl_3$, and (PhO)$_3$PO of 0.5 to 25 wt %), or AEEA vapor was passed through a bed of catalyst deposited on an inert carrier [39]. It was then mixed with an organic solvent (PhH or 1,4-dioxane), and the PP hydrate was distilled off azeotropically with a yield of 41−43%. AEEA (1.5 mol) transforms into PP in anhydrous toluene over 24 h under the action of an equimolar amount of Ph$_3$P(OEt)$_2$ at a temperature of 60°C with a yield of 50% [40]. It transforms into PP with a yield of 90% in absolute CCl_4 and an inert atmosphere over 20 h under the action of an equimolar amount of PCl_5 at temperatures of 30−60°C [41]. A disadvantage of these two processes is the use of phosphorus compounds, the wastes of which must be disposed of alongside hydrochloride (Table 2, entries 2−4).

There ways of PP production by catalytic AEEA cyclodehydration (1.4 mol) on heterogeneous catalysts through boiling (244°C) with Raney Ni (3.3 wt %) for 2.5 h inside a reaction vessel at atmospheric pressure with subsequent distillation of the product [12, 42]. The yield of the product is low at 32%. The yield of PP can be raised to 44% if the reaction proceeds in an autoclave with AEEA (0.32 mol) and Raney Ni (12 wt %) for 3.5 h at a H_2 pressure of 2.7−4.1 MPa and a temperature of 190−200°C. The yield of PP is 50% if the reaction is conducted with an AEEA solution (1.5 mol) in 1,4-dioxane (12.3 mol) to raise the loading of Raney Ni catalyst to 19.2 wt % at a temperature of 200°C in 3 h (Table 2, entries 5−7, 69).

Table 2. Catalytic ways of preparing PP based on intramolecular cyclization

No.	Components (ratios)	Catalyst (wt %)	H_2 pressure, MPa	T, °C	Reaction time, h	Yield of PP, %	Side products, (solvent)	Ref.
1	2	3	4	5	6	7	8	9
(a) Catalytic cyclodehydration of AEEA								
1[1)]	AEEA/H_2O	$[Cp^*IrCl_2]_2$ (0.25%)	—	140	48	79	—	[38]
2		H_3PO_4 (1%)	—	245	6	43	—	[39]
3		$Ph_3P(OEt)_2$	—	60	24	50	—, (PhMe)	[40]
4	AEEA	PCl_5	—	30–60	20	90	—, (CCl_4)	[41]
5		Raney Ni (3.3%)	—	244	2.5	32	Resins	[42]
6		Raney Ni (12%)	2.7–4.1	190–200	3.5	44	—	[12]
7		Raney Ni (19.2%)	—	200	3	50	Resins (1,4-Dioxane)	[42]
8	AEEA/NH_3(1/4.46)	20%Co/γ-Al_2O_3 (13.8%)	10	200	8	54.2	EDA, DETA etc.	[43]
9	AEEA	63%Cu/γ-Al_2O_3	—	220	1	95	—	[44]
10			3	180–190	—	85	—, (PhMe)	[45]
11	50% AEEA–H_2O	HZSM-280	—	350	2	80	—	[46]
12	AEEA·6H_2O	(7–10%)Cu/Raney Ni (10%)	3	180	3	79.1	—	[47]
13	45% AEEA–H_2O	Ni, Cu, Cr, Mn, Zn, Fe /γ-Al_2O_3	3	220	—	80	—, (1,4-Dioxane, THF, and EtOH)	[48]
14	AEEA	Cu,Cr,Fe/γ-Al_2O_3	0.1	180–280	720	93.6–95.1	—	[49]
15		Cu, Cr, La/γ-Al_2O_3 (15%)		170	100	98.6	—, (1,4-Dioxane)	[50]
16			3	160	300	89.7	N-Pr^{i}PP, (Pr^{i}OH)	[50]

Table 2. (Contd.)

No.	Components (ratios)	Catalyst (wt %)	H_2 pressure, MPa	T, °C	Reaction time, h	Yield of PP, %	Side products, (solvent)	Ref.
1	2	3	4	5	6	7	8	9
(b) Catalytic cyclodeamination of DETA								
17	DETA	Raney Ni (9.7%)	—	207	10	46	TEPA	[56]
				208	12	53	TEPA (tetralin)	
				160	8	63	TEPA (dipentene)	
18[2]	DETA/NH_3	Ni/E_xO_y (E are elements of V or VI groups)	4	185–210	—	91−92	PEA	[57]
19	DETA·HCl/ DETA−H_2O (92%)	—	—	210−240	—	50.7	EDA and H_2O	[58]
20	DETA	$H_3PO_4/\gamma\text{-}Al_2O_3$	—	330	—	20	EDA and PEA	[59]
21	DETA/EDA (1/1), 63 wt. % in H_2O	KZSM-5	—	360	—	63	TEDA	[60]
(c) Catalytic cyclohydrogenation of IDAN								
22	IDAN	Raney Ni (28%), H_2PtCl_6 (1%)	0.3	36	2	40.7	DETA	[61]
23	IDAN/NH_3(1.05/8.9)	Raney Ni	31	75	—	60	DETA	[62]
	IDAN/NH_3(0.36/22.7)		27.5−31	95−105	4	85		
(d) Catalytic hydrogenation of PR								
24[3]	PR/H_3SiPh (1/3)	$[Rh(nbd)(PPh_3)_2]PF_6$ (3% mol.)	—	82	24	100	— (Pr^iOH)	[64]
25	PR	Rh@Fe_3O_4 (1)	3	130	14	>99	— (H_2O)	[65]
26	PR	$[(\eta^5\text{-}C_5Me_5)Rh(NC)H]$ (1% mol.)	3.6	100	48	87	—	[66]

[1] $NaHCO_3$ additive (2 wt %).
[2] Amount of NH_3 (1−1.5 wt %).
[3] 0.5 eq. K_2CO_3 as additive.

Slightly better results were obtained (Table 2, entry 8) by converting AEEA (0.48 mol) with liquefied NH_3 (2.14 mol) on a 20% Co/γ-Al_2O_3 catalyst (13.8 wt %) inside a rotating autoclave for 8 h at 200°C and a H_2 pressure of 10 MPa. The yield of PP was 54.2% [43].

PP can be synthesized continuously via the reaction of AEEA on a 63%Cu/γ-Al_2O_3 catalyst inside a flow tubular reactor at a temperature of 220°C and atmospheric pressure (Table 2, entry 9), along with H_2 to maintain the activity of the catalyst. AEEA is completely converted during the first hour of catalyst operation, and the selectivity toward PP is 95%. The catalyst is then deactivated irreversibly [44]. AEEA was cyclized on the same catalyst in a PhMe solution at a temperature of 180−190°C and a H_2 pressure of 3 MPa. The yield of PP was 85% [45].

Good results were obtained during the vapor−gas phase catalytic dehydration cyclization of a 50% AEEA aqueous solution in a flow reactor on zeolites at temperatures of 260−400°C and atmospheric pressure [46]. The HZSM-280 catalyst gave the best results after 2 h of operation at 350°C. The conversion of AEEA was 100%, and the selectivity toward PP was 80% (Table 2, entry 11).

A variety of catalysts were tested in the dehydration and cyclization of AEEA·$6H_2O$ (20 mol) inside an autoclave to synthesize PP [47]. Different oxometalates of the Keggin heteropoly acid type and their salts were tested: $(NH_4)_3PW_{12}O_{40}$, $H_3PMo_{12}O_{40}$, $H_3PW_{12}O_{40}$, $H_4SiW_{12}O_{40}$, H_3PO_4, $Na_4P_2O_7$, and Cu, Cr, Fe, Ni, La, and Zn metals supported on γ-Al_2O_3 or such bulk catalysts as Ni-Raney and Cu-Raney. The most effective catalyst was 7−10% Cu/Raney Ni. The conversion of AEEA was 89.7%, while the selectivity and yield of PP were 88.2 and 79.1%, respectively, at a temperature of 180°C and a H_2 pressure of 3 MPa after 3 h of using this catalyst (10 wt %). The purity of the product was more than 98% after fractional distillation (Table 2, entry 12).

A catalyst is sometimes modified with such metals as (1−15%) Ni, (1−15%) Cu, (1−15%) Cr, (1−15%) Mn, (1−11%) Zn, and (2−10%) Fe supported on γ-Al_2O_3, while 20−60% AEEA aqueous solutions mixed with organic solvents (1,4-dioxane, tetrahydrofuran or EtOH) are used at temperatures of 190−220°C at a H_2 pressure of 3−3.5 MPa in a continuous flow vapor−gas phase process to improve the efficiency of the reaction (Table 2, entry 13). The conversion of AEEA is 86%, while the selectivity and yield of PP are 93 and 80%, respectively [48].

The best indicators were obtained in a flow tubular reactor on a Cu-Cr-Fe/γ-Al_2O_3 catalyst at temperatures of 180−280°C and H_2 atmospheric pressure after 30 days of catalyst operation [49]. The AEEA conversion was no less than 98.5%, and the selectivity and yield of PP were 95−96.5 and 93.6−95.1%, respectively (Table 2, entry 14).
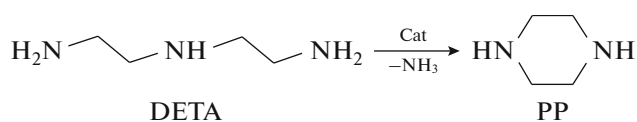
Fig. 8. Scheme of PP synthesis by catalytic DETA cyclodeamination.

A variety of catalysts (20%Cu/γ-Al_2O_3, 20%Cu, 10%Cr)/γ-Al_2O_3 and (20%Cu, 10%Cr, 10%La)/γ-Al_2O_3 were tested in synthesizing PP with AEEA solution (15 wt %) inside a continuous reactor. The best indicators were obtained using a (20%Cu, 10%Cr, 10%La)/γ-Al_2O_3 catalyst at a temperature of 170°C and a H_2 pressure of 3 MPa over 100 h. The conversion of AEEA was 99.5%, and the selectivity and yield of PP were 99.1 and 98.6%, respectively [50]. If alcohols were used, they acted as both a solvent and an alkylation agent. The best results were obtained with an AEEA solution (15 mol %) in Pr^iOH at a temperature of 160°C and a H_2 pressure of 3 MPa over 300 h. The conversion of AEEA was 98.6%, and the yield of PP was 89.7% (Table 2, entries 15−16) [51].

It should be noted that the initial AEEA can be obtained via the catalytic dimerization of MEA [7, 52] through the action of ethyleneimine on MEA hydrochloride [53], ethylene oxide on EDA [54], and the catalytic hydroamination of DEA [55].

2.2. Preparing PP by DETA Cyclodeamination

Processes for PP synthesis by catalytic DETA cyclodeamination are conducted periodically and continuously. Figure 8 shows the scheme of synthesis.

PP can be obtained in a few hours via the catalytic cyclodeamination of DETA (1 mol) dissolved in a hydrocarbon (the solvent reduces the formation of high-boiling resinous residues) at a temperature comparable to the boiling point of the solvent when using Raney Ni (9.7 wt %) [56]. The target product was isolated via distillation. The authors found that the yield of the product depends on the solvent that is used. The best results were obtained in 12 h using tetralin at 208°C (reflux) (the yield of PP was 53%) and in 8 h using dipentene in an autoclave at 160°C (the yield of PP was 63%) (Table 2, entry 17). It should be noted that the yield of PP was only 46% after 10 h with no solvent (DETA boils at 207°C; reflux). The authors noted that the synthesis of PP from EDA probably proceeds through an intermediate stage of DETA formation, but the yield of PP is no more than 10−13% [56].

A process was developed for the deamination of DETA containing dissolved NH_3 (1−1.5 wt %). The reaction was conducted in a flow-through installation that contained a cascade of autoclaves, using Ni catalyst deposited on oxides of elements of group V or VI of the periodic system. The DETA conversion was
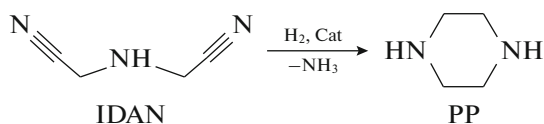
Fig. 9. Scheme of PP synthesis by catalytic IDAN cyclohydrogenation.

73.5–95% at a temperature of 185–210°C, a H_2 pressure of 4 MPa, and a contact period of 0.9 h. The yield of PP was 91–92% [57].

A 92% aqueous solution of DETA was added to the melt of a dry DETA hydrochloride salt obtained from a DETA and NH_4Cl aqueous solution taken in equimolar amounts after the evaporation of NH_3 and water. The reaction proceeded on the contact surface at temperatures of 210–240°C. The conversion of DETA was complete. The 130–170°C fraction of 50.7% PP was taken from the reaction solution [58].

The kinetics of catalytic gas-phase deamination of DETA was studied using a flow reactor at temperatures of 330–380°C on ZSM-5, γ-Al_2O_3, and γ-Al_2O_3 zeolites impregnated with reagents normally used for liquid-phase processes: H_3PO_4, NH_4F, Cr_2O_3, NiO, and MoO_3 in amounts of 5 wt % [59]. The activity was higher for acid catalysts, and the maximum was for H_3PO_4/γ-Al_2O_3. The selectivity of PP, however, was no more than 20% at full conversion of DETA. It should be noted that low temperatures promote deamination, while higher ones allow subsequent dehydrogenation.

Good results were obtained for the deamination of a DETA aqueous solution with EDA taken in an equimolar ratio with a total concentration of 63 wt % inside a flow tubular reactor on KZSM-5 catalyst at a temperature of 360°C and a pressure of 5 MPa (Table 2, entry 21). The conversion of DETA was 100%, and that of EDA was 28%. The selectivity toward PP was 85%, and its yield was 63% [60].

Table 2 (subgroup b) presents data on the synthesis of PP by catalytic DETA cyclodeamination. The highest yield of PP (91–92%) is seen for the process performed in a flow reactor on Ni catalysts supported on metal oxides. Advantages of such procedures are high selectivity. A disadvantage is the formation of waste (PEA) from which it is difficult to extract PP, which raises the cost of production.

2.3. Preparing PP by IDAN Cyclohydrogenation

Processes for PP synthesis by catalytic IDAN cyclohydrogenation are conducted according to the scheme shown in Fig. 9.

A batch process for preparing PP with a yield of 40.7% is based on the reduction of IDAN (0.67 mol) dissolved in absolute EtOH for 2 h at a temperature of 36°C and a H_2 pressure of 0.3 MPa using Raney Ni W-2 (28 wt %) and 1% H_2PtCl_6 as a promoter in a shaken autoclave. A product of the complete reduction of DETA is created, but it does not transform into PP under the specified conditions of the reaction [61].

PP was synthesized continuously through the reaction of a mixture of 10 wt % IDAN (1.05 mol) with 10 wt % NH_3 (8.59 mol) in MeOH (44.55 mol) (EtOH or tetrahydrofuran can be used) in a flow tube reactor on a Raney Ni catalyst at a temperature of 75°C and a H_2 pressure of 31 MPa. The fraction of boiling at 139–142°C was removed via distillation, and the yield of PP was 60%. The best results were obtained by reducing IDAN (0.36 mol) in NH_3 (22.7 mol) for 4 h with a Raney Ni catalyst in a steel autoclave at temperatures of 95–105°C and a H_2 pressure of 27.5–31 MPa. The product was isolated via distillation. The yield of PP with low amounts of DETA was 85% [62]. The initial IDAN for these processes can be obtained via the cold condensation of urotropine with HCN using HCl [63].

Table 2 (subgroup c) presents data on preparing PP via the catalytic cyclohydrogenation of IDAN. They show a periodic process with a high amount of NH_3 provides high yields of PP (85%, entry 23). An advantage of this process is a high yield of PP; a disadvantage is the use of high pressure.

2.4. Preparing PP by Pyrazine Reduction

PP can be produced by catalytic PR hydrogenation (Fig. 10) using a periodic process inside a mixing reactor (autoclave) or integral-type flow reactors.

In principle, PR can be hydrogenated with gaseous H_2 using metal complex catalysts or through reduction in EtOH using metallic Na or Ni-Al alloy in KOH solutions. The yields of PP are more than 76% [64–68]. The initial PR for such processes can be obtained via the catalytic cyclodehydration dehydrogenation of AEEA or the cyclodeamine dehydrogenation of DETA.

The authors of [65] described the hydrogenation of nitrogen-containing heterocyclic precursors in aqueous media at low temperatures without H_2 pressure. Synthesis proceeds with tetrahydroxydiboron $B_2(OH)_4$ as a reduction agent in water at 80°C using a catalyst containing Rh. Subnano-range (<1 nm) rhodium particles were obtained in situ via the reduction of a Rh precursor on freshly prepared superparamagnetic iron oxide nanoparticles (SPION, Fe_3O_4) using NH_3 aqueous solution as a reduction agent at 50°C (Table 2, entry 25). This catalyst was also highly efficient in the heterogeneous hydrogenation of nitrogen-containing heterocyclic compounds with quantitative conversion. It was found it can be used for 16 consecutive cycles with hydrogen gas without any undesirable by-products while retaining its original crystallinity.

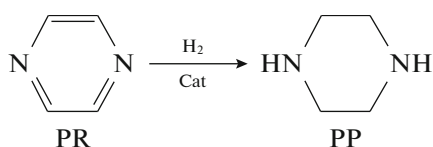Conventional complex hydrogenation substrates *N*-heteroarenes (pyridine, pyrrole, and pyrazine) were

Fig. 10. Scheme of PP synthesis by catalytic PR hydrogenation.

hydrogenated on homogeneous organometallic precatalysts $[(\eta^5\text{-}C_5Me_5)Rh(NC)H]$, where NC = 2-phenylpyridinyl (ppy) or benzo[h]quinolinyl (bq) [66]. They transformed into catalytically active multimetallic clusters when hydrogen was used (Table 2, entry 26). The yield of the target product was 87%.

Another metal complex catalyst $[\{(\eta^6\text{-cymene})RuCl\}_2\text{-}(\mu\text{-}H-\mu\text{-}Cl)]$ was proposed in [67]. PIR was hydrogenated at room temperature, a H_2 pressure of 5 MPa in a nitrogen atmosphere, and in 1,4-dioxane as a solvent. The yield of PP was 87%.

PIR can also be hydrogenated by using Ni-Co nanoparticles (1 : 1) deposited on SiO_2 [68]. The temperature of the reaction is 80°C, the H_2 pressure is 5 MPa, and the solvent is isopropanol. The yield of PP is 99%.

The catalytic hydrogenation of PIR on metal complex catalysts with an organic component or catalysts supported on ferromagnetic supports ensures a maximum yield of PP that is close to 100%, compared to any other means (Table 2, subgroup g). However, these studies are still at the laboratory level. It should also be remembered that PIR is a more expensive raw material than PP, so the process could be unprofitable.

CONCLUSIONS

The piperazine (PP) production methods based on intermolecular and intramolecular catalytic processes have certain features:

—The lowest yields of PP (around 31.5%) are observed when using ethylene glycol (EG) with NH_3 as the raw material.

—Preparing PP with average yields of 55—60, 62, and 67% allows the use of mono- or diethanolamine and ammonia.

—The greatest yields of PP (80—85%) are obtained using ethylenediamine, ethylenediamine with EG, and iminodiacetonitrile with ammonia as raw materials.

—High yields of PP (92 and 95%) are achieved when using diethylenetriamine and aminoethylethanolamine as raw materials.

These processes would seem to be the ones most effective, due to the relatively milder conditions of synthesis, fewer by-products, and thus minimal costs of isolating and purifying target products and disposing waste, which corresponds to the concepts of green chemistry and sustainable development.

We can generally recommend batch-type processes that use homogeneous and heterogeneous catalysts for the medium- and small-scale production of an import substitute product (piperazine) and continuous vapor—gas phase processes on heterogeneous catalysts for large-scale production (Tables 1 and 2).

It should also be noted that catalytic processes conducted in continuous mode in the vapor—gas phase and proceeding with high conversion but poor selectivity toward the target product (piperazine) can be used in an integrated approach to organizing them. This is because many by-products (and/or intermediates) are of separate importance and in demand. For example, EDA is used to prepare fungicides, surfactants, and plasticizers; polyethylene polyamides are components of an additive that increases the moisture resistance of paper products, and DETA is used as a catalyst in the production of polyurethanes.

APPENDIX A

AEEA—aminoethylethanolamine
DCE—1,2-dichloroethane
DEA—diethanolamine
DETA—diethylenetriamine
IDAN—iminodiacetonitrile
MOR—morpholine
MEA—monoethanolamine
PP—piperazine
PR—pyrazine
PEA—polyethyleneamines
TEDA—triethylenediamine
TEPA—tetraethylenepentamine
EG—ethylene glycol
EDA—ethylenediamine

REFERENCES

1. *Piperazin: Sbornik statei/AN Latviiskoi SSR* (Piperazine: Collection of Papers/AN Latvian SSR), Giller, S.A. and Shimanska, M.V., Eds., Riga: Zinatne, 1965.

2. GNITIVE Marker Research. Global Piperazine—PIP Market Report 2022. https://www.cognitivemarket-research.com/chemical-%26-materials/piperazine-%28 pip%29-market-report. Cited April 17, 2022.

3. Sridhar, S. and Carter, R.G., in: *Kirk-Othmer Encyclopedia of Chemical Technology,* New York: Wiley, 2001. https://doi.org/10.1002/0471238961.04090113030118 20.a01.pub

4. Roose, P., Eller, K., Henkes, E., Rossbacher, R., and Höke, H., in: *Ullmann's Encyclopedia of Industrial Chemistry,* Weinheim: Wiley-VCH, 2015.
https://doi.org/10.1002/14356007.a02_001.pub2

5. Shimanskaya, M.V., Oshis, Ya.F., and Anderson, A.A., *Chem. Heterocycl. Compd.,* 1983, vol. 19, no. 12, pp. 1249−1262.

6. KR Patent 20170041077, 2017.

7. Lei, M., Li, Y., An-Hui, L., and Yunjie, D., *RSC Adv.,* 2018, vol. 8, no. 15, pp. 8152−8163.
https://doi.org/10.1039/c7ra12891f

8. Borisenko, V.S., Bobylev, V.A., and Tereshchenko, G.F., *Zh. Obshch. Khim.,* 1985, vol. 55, no. 5, pp. 1141−1146.

9. Borisenko, V.S., Bobylev, V.A., Selivanov, S.I., Utsal', V.A., and Tereshchenko, G.F., *Zh. Obshch. Khim.,* 1986, vol. 56, no. 10, pp. 2339−2345.

10. Jpn. Patent 6301695, 2018.

11. Clapp, L.B., *J. Am. Chem. Soc.,* 1948, vol. 70, no. 1, pp. 184−186.
https://doi.org/10.1021/ja01181a053

12. Ishiguro, T., Kitamura, E., and Matsumura, M., *J. Pharm. Soc. Jpn.,* 1957, vol. 77, no. 10, pp. 1051−1054.
https://doi.org/10.1248/yakushi1947.77.10_1051

13. USSR Inventor's Certificate no. 166033, *Byull. Izobret.,* 1964.

14. Ishiguro, T., Kitamura, E., Matsumura, M., and Ogawa, H., *J. Pharm. Soc. Jpn.,* 1955, vol. 75, no. 11, pp. 1318−1321.
https://doi.org/10.1248/yakushi1947.75.11_1318

15. Sasaki, T., *J. Synt. Org. Chem., Jpn.* 1958, vol. 16, no. 11, pp. 614−620.
https://doi.org/10.5059/yukigoseikyokaishi.16.614

16. Balandin, A.A., Karpeiskaya, E.I., Ferapontov, V.A., and Tolstopyatova, A.A., *Dokl. Akad. Nauk SSSR,* 1965, vol. 165, no. 1, pp. 99−102.

17. Balandin, A.A., Ferapontov, V.A., Karpeiskaya, E.I., Gorshkova, L.S., and Tolstopyatova, A.A., *Dokl. Akad. Nauk SSSR,* 1966, vol. 168, no. 5, pp. 1061−1064.

18. Sun, Y., *J. Chem. Eng. Chin. Univ.,* 1999, vol. 13, no. 2, pp. 178−181.

19. US Patent 4234730, 1980.

20. Jiangang, L., Jiansheng, L., Xiuyun, S., and Lianjun, W., *Petrochem. Technol. (China),* 2004, vol. 33, no. 9, pp. 861−864.

21. Zhang, Y., Bai, G., Yan, X., Li, Y., Zeng, T., Wang, J., Wang, H., Xing, J., Luan, D., Tang, X., and Chen, L., *Catal. Commun.,* 2007, vol. 8, no. 7, pp. 1102−1106.
https://doi.org/10.1016/j.catcom.2006.10.018

22. Shang, H., Wang, L., Wang, S., Gao, P., and Zheng, X., *Chem. React. Eng. Technol. (China),* 2012, vol. 28, no. 2, pp. 188−192.

23. Jpn. Patent 5803619, 2013.

24. Corma, A., Ródenas, T., and Sabater, M.J., *Chem.—Eur. J.,* 2010, vol. 16, no. 1, pp. 254−260.
https://doi.org/10.1002/chem.200901501

25. Jenner, G. and Bitsi, G., *J. Mol. Catal.,* 1988, vol. 45, no. 2, pp. 165−168.
https://doi.org/10.1016/0304-5102(88)80005-1

26. US Patent 3068232, 1962.

27. Yang, Z., Gong, F., and Qi, Y., *Chem. React. Eng. Technol. (China),* 2016, vol. 32, no. 6, pp. 570−575.

28. Weitkamp, J., Ernst, S., Buysch, H.-J., and Lindner, D., *Stud. Surf. Sci. Catal.,* 1991, vol. 65, pp. 297−304.
https://doi.org/10.1016/S0167-2991(08)62914-6

29. Sun, S.-H., Shen, W., Xu, H.-L., Zhou, Y.-M., Xiang, Y., and Liu, J.-X., *Chin. J. Catal.,* 1998, vol. 19, no. 5, pp. 432−435.

30. Liu, R.-J., Bao, J.-Y., Zhang, Y., Tian, Z., and Wei, Z.-X., *Chem. Eng. (China),* 2006, vol. 34, no. 6, pp. 68−71.

31. Wei, X.-X., Tian, Z.-S., Liang, J.-G., Liu, R.-J., Hao, H., and Wei, N.-N., *Chem. Eng. (China),* 2012, vol. 40, no. 1, pp. 56−58.

32. Gen-zhi, G., Yan-xin, L., Bin, Z., and Xiao-feng, Z., *J. Petrochem. Univ. (China),* 2006, vol. 19, no. 3, pp. 48−50.

33. Ishiguro, T., Kitamura, E., and Matsumura, M., *J. Pharm. Soc. Jpn.,* 1953, vol. 73, no. 10, pp. 1110−1114.
https://doi.org/10.1248/yakushi1947.73.10_1110

34. Sasaki, T., *J. Synt. Org. Chem., Jpn.,* 1959, vol. 17, no. 1, pp. 17−28.
https://doi.org/10.5059/yukigoseikyokaishi.17.17

35. Kliger, G.A., Fidler, Kh., Lesik, O.A., Khabish, D., Khlebov, L.S., Zaikin, V.G., Khaage, K., and Loktev, S.M., *Neftekhimiya,* 1988, vol. 28, no. 5, pp. 684−694.

36. US Patent 8981093, 2015.

37. Ishiguro, T., Kitamura, E., Matsumura, M., and Ogawa, H., *J. Pharm. Soc. Jpn.,* 1955, vol. 75, no. 11, pp. 1367−1369.
https://doi.org/10.1248/yakushi1947.75.11_1367

38. Lorentz-Petersen, L.L.R., Nordstrøm, L.U., and Madsen, R., *Eur. J. Org. Chem.,* 2012, vol. 34, pp. 6752−6759.
https://doi.org/10.1002/ejoc.201201099

39. US Patent 3112317, 1963.

40. Kelly, J.W., Eskew, N.L., and Evans, S.A.Jr., *J. Org. Chem.,* 1986, vol. 51, no. 1, pp. 95−97.
https://doi.org/10.1021/jo00351a020

41. CN Patent 102442957, 2016.

42. Kitchen, L.J. and Pollard, C.B., *J. Am. Chem. Soc.,* 1947, vol. 69, no. 4, pp. 854−855.
https://doi.org/10.1021/ja01196a034

43. Karpeiskaya, E.I., Ferapontov, V.A., Tolstopyatova, A.A., and Balandin, A.A., *Russ. Chem. Bull.,* 1968, vol. 17, no. 7, pp. 1419−1424.
https://doi.org/10.1007/BF00907837

44. Hammerschmidt, W., Baiker, A., Wokaun, A., and Fluhr, W., *Appl. Catal.,* 1986, vol. 20, nos. 1−2, pp. 305−312.
https://doi.org/10.1016/0166-9834(86)80022-7

45. Chen, L.-G., Song, Y., Xu, Z.-S., Wang, D.-L., and Meng, Y., *Chem. Ind. Eng. (China),* 2001, vol. 18, no. 1, pp. 40−43.

46. Subrahmanyam, M., Kulkarni, S.J., and Srinivas, B., *React. Kinet. Catal. Lett.,* 1993, vol. 49, no. 2, pp. 455−459.
https://doi.org/10.1007/BF02067715

47. Wu, G.-J. and Yan, Z.-G., *J. East China Univ. Technol., Nat. Sci.,* 2001, vol. 27, no. 1, pp. 30−33.

48. CN Patent 100334078, 2007.

49. Bai, G.Y., Li, Y., Yan, X.L., He, F., and Chen, L.G., *React. Kinet. Catal. Lett.,* 2004, vol. 82, no. 1, pp. 33−39. https://doi.org/10.1023/b:reac.0000028802.66602.0f

50. Wu, Z., Yang, F., Wang, H., Ma, J., Chen, L., and Li, Y., *React. Kinet. Mech. Catal.,* 2012, vol. 106, no. 2, pp. 485−493. https://doi.org/10.1007/s11144-012-0447-z

51. Wu, Z., Wang, H., Sun, M., Du, X., Chen, L., and Li, Y., *Res. Chem. Intermed.,* 2012, vol. 38, nos. 3−5, pp. 1149−1157. https://doi.org/10.1007/s11164-011-0450-4

52. Ford, M.E., Johnson, T.A., Premecz, J.E., and Cooper, C.A., *J. Mol. Catal.,* 1988, vol. 44, no. 2, pp. 207−211. https://doi.org/10.1016/0304-5102(88)80032-4

53. Braz, G.I. and Skorodumov, V.A., *Dokl. Akad. Nauk SSSR,* 1948, vol. 59, no. 3, pp. 489−492.

54. Trejbal, J. and Petrisko, M., *React. Kinet. Catal. Lett.,* 2004, vol. 82, no. 2, pp. 339−346. https://doi.org/10.1023/b:reac.0000034846.59643.e6

55. WO Patent 2013095810, 2013.

56. Martin, W.B. and Martell, A.E., *J. Am. Chem. Soc.,* 1948, vol. 70, no. 5, pp. 1817−1818. https://doi.org/10.1021/ja01185a049

57. USSR Inventor's Certificate no. 467073, *Byull. Izobret.,* 1975.

58. USSR Inventor's Certificate no. 539881, *Byull. Izobret.,* 1976.

59. Bhat, Y.S., Kulkarnl, B.D., and Doralswamy, L.K., *Ind. Eng. Chem. Process Des. Dev.,* 1985, vol. 24, no. 3, pp. 525−530. https://doi.org/10.1021/i200030a00

60. Jpn. Patent 6638364, 2020.

61. Mosher, H.S., Cornell, J.Jr., Stafford, O.L., and Roe, T., *J. Am. Chem. Soc.,* 1953, vol. 75, no. 20, pp. 4949−4951. https://doi.org/10.1021/ja01116a020

62. US Patent 2809196, 1957.

63. SU Patent 697501, *Byull. Izobret.,* 1979, no. 42.

64. Voutchkova, A.M., Gnanamgari, D., Jakobsche, C.E., Butler, C., Miller, S.J., Parr, J., and Crabtree, R.H., *J. Organomet. Chem.,* 2008, vol. 693, no. 10, pp. 1815−1821. https://doi.org/10.1016/j.jorganchem.2008.02.004

65. Nasiruzzaman, M.S., Abdul, M.A., Kalanthoden, A.N., Helal, A., Hakeem, A.S., and Bououdina, M., *Catal. Sci. Technol.,* 2018, vol. 8, no. 18, pp. 4709−4717. https://doi.org/10.1039/c8cy00936h

66. Kim, S., Loose, F., Bezdek, M.J., Wang, X., and Chirik, P.J., *J. Am. Chem. Soc.,* 2019, vol. 141, no. 44, pp. 17900−17908. https://doi.org/10.1021/jacs.9b09540

67. Chatterjee, B., Kalsi, D., Kaithal, A., Bordet, A., Leitner, W., and Gunanathan, C., *Catal. Sci. Technol.,* 2020, vol. 10, pp. 5163−5170. https://doi.org/10.1039/D0CY00928H

68. Ciotonea, C., Hammi, N., Dhainaut, J., Marinova, M., Ungureanu, A., El Kadib, A., Michon, C., and Royer, S., *ChemCatChem*, 2020, vol. 12, no. 18, pp. 4652−4663. https://doi.org/10.1002/cctc.202000704

69. Lei, M., Li, Y., An-Hui, L., and Yunjie, D., *Chin. J. Catal.,* 2019, vol. 40, no. 4, pp. 567−579.

Translated by A. Tulyabaev