An efficient synthesis of *N,N,N',N',N''*-Pentamethyldipropylenetriamine

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N,N,N',N',N''-Pentamethyldipropylenetriamine (PMDPTA) has for a long time been employed as an efficient catalyst in the production of polyurethane materials. A green and effective synthetic route to PMDPTA was successfully established from experiments described in this paper. PMDPTA was obtained from methylamine, acrylonitrile and formaldehyde *via* a Michael addition, catalytic hydrogenation and methylation in 65% overall yield. Furthermore, methanol was employed as the only solvent in all of the three steps, resulting in the convenient recovery of methanol. This route is thus suitable for industrial production..

Keywords: N,N,N',N',N''-pentamethyldipropylenetriamine, PMDPTA, Michael addition, catalytic hydrogenation, methylation

Polyurethane (PU) foams are an important type of polymeric material and have been extensively used in a variety of applications in the building, shipping, automobile and textile industries. Their excellent foaming ability, flexibility, adhesion and low-temperature resistance make them very versatile both in industrial manufacturing and in civil use as elastomers, foams, coatings, adhesives, waterproofing materials and many other uses.

Polyurethane materials are usually prepared from polyisocyanate and polyols with different molecular weights and functionalities. Moreover, auxiliary agents such as catalysts, and flame retardants are also needed in accordance with industrial requirements. The required catalysts normally play an important role in the PU foam formation, not only accelerating the reaction but also improving the physical properties of the polymer products.[1,2] Organometallic compounds like organotin compounds are a major kind of catalyst for the production of polyurethanes while organic amines are other efficient and convenient catalysts, especially the aliphatic tertiary amines like triethylenediamine (TMDA), diethylenetriamine (DMTA) and *N,N,N',N',N''*-pentamethyldipropylenetriamine (PMDPTA).[3] As an efficient catalyst for the production of PU materials, PMDPTA has been used for decades It has found some useful applications in other fields. It was recently reported that PMDPTA is a key component of a radiation curable inkjet ink[4] and Thurner claimed that PMDPTA could efficiently enhance the lithiation reactions for site selective metallation of aromatic and heteroaromatic compounds.[5]

Surprisingly, there is currently no complete synthetic route to PMDPTA found in the literature. The reported synthesis of PMDPTA is the simple methylation reaction of 3,3'-iminobis(*N,N*-dimethylpropylamine) with formaldehyde in the presence of formic acid,[6] which suffers from high cost, low yield, environmental pollution and severe corrosion.

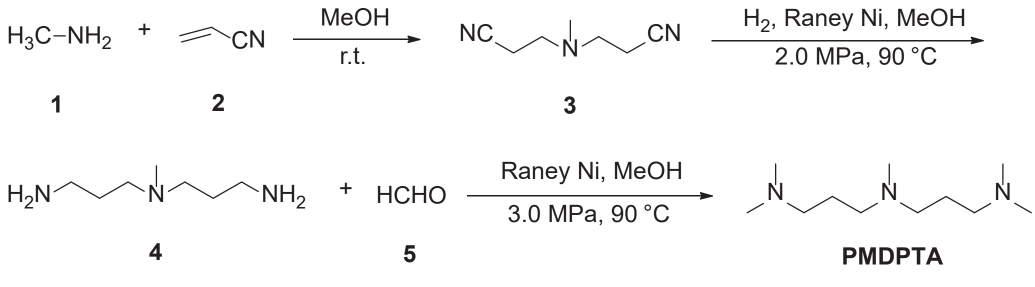
Herein, we describe a novel synthetic route to PMDPTA from methylamine, acrylonitrile and formaldehyde *via* the Michael addition, catalytic hydrogenation and methylation (Scheme 1). In all of the three steps, methanol was selected as the only solvent thus making one-pot synthesis quite possible. The overall yield of the three-step sequence is 65%.

Results and discussion

It is well known that the Eschweiler–Clarke reaction causes serious pollution. Thus the synthesis of PMDPTA by the methylation of 3,3'-iminobis(*N,N*-dimethylpropylamine) with formaldehyde in the presence of formic acid has disadvantages and the catalytic methylation with formaldehyde in a hydrogen atmosphere is preferable. With the considerations of a more eco-friendly catalytic hydrogenation and the ease of Michael addition of methylamine and acrylonitrile,[7] the synthetic route described in Scheme 1 was selected for PMDPTA.

Initially, based on the reported works, the Michael addition of methylamine (**1**) and acrylonitrile (**2**) was systematically examined. It was found that the yield of *N,N*-bis(2-cyanoethyl) methylamine (**3**) increased with an increase in temperature with an optimum temperature of 25 °C. Meanwhile, the molar ratio of acrylonitrile and methylamine was evaluated and the results obtained indicated that 2.2:1 was promising. As mentioned above, the reaction parameters were optimised, so under the optimised conditions, 100% conversion of methylamine and 95% selectivity of compound **3** were obtained. Methanol was conveniently used as the solvent. The resulting Michael addition adduct in methanol solution was used directly in the next catalytic hydrogenation step without further purification.

The catalytic hydrogenation of aliphatic nitriles to the corresponding aliphatic amines is a powerful tool in organic



Scheme 1 The synthetic route to PMDPTA.

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synthesis and has been intensively studied.[8–11] Chen reported that[11] some by-products, including amino-nitriles, diimines and homopiperazines could be detected during the catalytic hydrogenation. The reaction temperature and the pressure of hydrogen played a critical role in the formation of these by-products. The influence of reaction temperature on the hydrogenation reaction was first examined and the results indicated that the selectivity in formation of compound **4** gradually increased with the increase in the reaction temperature. Thus, 90 °C was selected as the suitable reaction temperature. Furthermore, the effect of hydrogen pressures was also evaluated and it was discovered that the conversion of compound **3** and the selectivity of formation of compound **4** increased with the increase of hydrogen pressures. Thus, 2.0 MPa was found to be satisfactory.

The catalyst has a significant influence on the reactivity of the hydrogenation reaction. Three hydrogenation catalysts including W-3 Raney Ni, TLD-A and Al–Ni–Mo were studied respectively and the results showed that W-3 Raney Ni exhibited better catalytic performance compared to the others. The 100% reaction of compound **3** and the 85% selectivity of formation of compound **4** were obtained when W-3 Raney Ni was used while 68% and 76% yields were respectively achieved when TLD-A and Al-Ni-Mo were employed. In addition, Liu reported that the presence of a base was beneficial in increasing the activity of Raney Ni.[8,9] Therefore, sodium hydroxide in this reaction was added in order to accelerate the reaction and increase the yield.

Finally, the influence of the solvents on the reactivity was also examined. The 100% conversion of compound **3** and the 85% selectivity in formation of compound **4** were obtained when absolute ethanol was used as the solvent, while the 67% yield was achieved when methanol was employed. It suggests that the solvent with weaker polarity was more favourable for the catalytic hydrogenation. Nevertheless, methanol was employed in the first step and only a moderate yield was gained in the second step. However, a one-pot reaction can be realised by using the same solvent which has the features of a simple operation and the possibility of recycling in industrial applications. Thus, methanol was selected as the optimal solvent. Without further purification the resulting methanol solution was used directly in the next methylation step.

The N–methylation of primary amines to the corresponding dimethyl tertiary amines has been widely studied[12–15] and the three main methods including the Eschweiler–Clarke reaction, methanol–hydrogenation, and formaldehyde–hydrogenation have been employed in industrial production. Although the Eschweiler–Clarke reaction had the advantage of mild operation conditions, formic acid is inevitably used. This method suffers from several defects such as low efficiency, environmental pollution and severe corrosion of equipment. Therefore, this method has been gradually eliminated in industrial practice. For the methanol–hydrogenation of primary amines, although excellent yields could be obtained, excessive hydrogen pressures and high reaction temperatures were required, leading to excessive demands of the equipment as well as high costs. Compared with the above methods, the formaldehyde–hydrogenation of primary amines has incomparable advantages including high efficiency and little pollution. Therefore, with the W-3 Raney Ni as a catalyst, 81.0% yield of PMDPTA was achieved by using compound **4** and an aqueous formaldehyde solution in methanol at 90 °C, and 3.0 MPa.

Conclusions

In conclusion, a green and effective synthetic route to PMDPTA was established. Under the optimised reaction conditions, PMDPTA was obtained from methylamine, acrylonitrile and formaldehyde in 65% total yield. Methanol was used as the solvent in all the three steps, leading to the convenient recovery of solvents. This synthetic route is thus, suitable for the industrial production of PMDPTA.

Experimental

Methylamine methanol solution, ethanol, methanol, acrylonitrile and aqueous formaldehyde solution were purchased from commercial sources and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker Avance (III) 400 MHz spectrometer using $CDCl_3$ as the solvent. High-resolution mass spectra (HRMS) were performed on a Bruker Daltonics miorOTOF-QII instrument. The composition of the reaction mixture was identified by GC-400A equipped with a OV-1701 column (30 m × 0.5 mm).

Synthesis of N,N-bis(2-cyanoethyl)methylamine (**3**)

Acrylonitrile (11.66 g, 0.22 mol) was added drop by drop into the methylamine methanol solution (12.7 mL, 0.1 mol) at 0 °C in 30 min while magnetically stirring. The reaction mixture was stirred for 4 h at 25 °C and then the volatile was evaporated to give **3**: light yellow liquid; 13.03 g, 95.0% yield; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.32 (s, 3H, CH_3), 2.48 (t, $J = 6.8$ Hz, 4H, CH_2), 2.76 (t, $J = 7.0$ Hz, 4H, CH_2).

Preparation of W-3 Raney Ni catalyst

Nickel–aluminium alloy powder (25 g) was added in batches to the sodium hydroxide aqueous solution (152 g, 20 wt%) at 40–50 °C whilst constantly stirring in a 500 mL beaker. The mixture was stirred at 50 °C for 1 h and then stirred at 25 °C for 24 h. After that, the upper aqueous phase of the stationary mixture was discarded. The catalyst was washed each time with distilled water (100 mL) until the pH value of the aqueous phase was 7 and then replaced with absolute ethanol by 3 times. The prepared catalyst was kept in a conical flask full of absolute ethanol.

Synthesis of N,N-bis(3-aminopropyl)methylamine (**4**)

Compound **3** (30 mL), ethanol (150 mL), sodium hydroxide (0.18 g) and W-3 Raney Ni (6 g) were added into the 300 mL autoclave. The air in the autoclave was replaced with nitrogen by 3 times and then with hydrogen by 3 times. The dangers of hydrogen/oxygen contact with the catalyst should always be given attention since a mixture of hydrogen and oxygen is capable of leading to an explosion. After the reaction mixture was stirred at 90 °C, 2.0 MPa, the reaction was not stopped until the hydrogen pressure no longer dropped over 6 h and then the mixture was filtered. When the mixture was filtered, Raney Ni should always be kept wet with ethanol and should never have direct contact with air since dry Raney Ni can easily burst into flames in the air, which could result in significant hazards. After the filtration, the solvent was evaporated to give **4**: viscous, colourless liquid; 25.5 g, 85.0% yield; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.65 (m, $J = 7.6$ Hz, 4H, CH_2), 2.26 (s, 3H, CH_3), 2.37 (t, $J = 7.4$, 4H, CH_2), 2.48 (t, $J = 7.4$ Hz, 4H, CH_2), 5.15 (s, 4H, NH_2).

Synthesis of N,N,N',N',N''-pentamethyldipropylenetriamine (PMDPTA)

Compound **4** (14.5 g, 0.1 mol), methanol (150 mL), aqueous formaldehyde solution (40.6 g, 0.5 mol, 37 wt%) and W-3 Raney Ni (3 g) were added to the autoclave. The air in the autoclave was replaced with nitrogen (3 times) and then with hydrogen (3 times). The dangers of hydrogen/oxygen contact with the catalyst should always be given attention since a mixture of hydrogen and oxygen is capable to of leading to an explosion. Then the reaction mixture was stirred at a rotation speed of 500 rpm at 90 °C, 3.0 MPa. The reaction was not stopped until the hydrogen pressure no longer dropped over 5 h and then the mixture was filtered. When the mixture was filtered, Raney Ni should always be kept wet with ethanol and should never directly have contact with the air since dry Raney Ni can easily burst into flames in the air which could result in significant hazards. After the filtration, volatiles were evaporated to give PMDPTA: viscous, yellow liquid; 16.28 g, 81.0% yield; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.63 (m, *J* = 7.6 Hz, 4H, CH_2), 2.21 (s, 15H, CH_3), 2.27 (t, *J* = 7.4 Hz, 4H, CH_2), 2.35 (t, *J* = 7.4 Hz, 4H, CH_2); ^{13}C NMR (CD_3OD, 151 MHz) δ: 57.3 (2 × C, CH_2), 55.2 (2 × C, CH_2), 44.1 (4 × C, CH_3), 40.9 (1 × C, CH_3), 24.2 (2 × C, CH_2); ESI–HRMS *m/z* $[M + H]^+$: calcd 202.2239, observed 202.2287.

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