Electronic Supplementary Material (ESI) for Green Chemistry.

One-pot production of phenazine from lignin-derived catechol

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1. Material and experimental procedures

1.1 Material

Chemicals: catechol (99%), 4-methylcatechol (95%), 4-ethylcatechol (95%), 3-methylcatechol (98%), 4-t-butylcatechol (97%), 2,3-Dihydroxynaphthalene (98%), 3-Methoxycatechol (99%), 2,3-dihydroxybenzoic acid (99%), pyrogallol (98%), 3,4-dihydroxybenzoic acid (97%), 3,4-dihydroxybenzaldehyde (97%), 3,4-dihydroxybenzonitrile (97%), phenazine (98%), 1,2-diaminocyclohexane (mixture of cis and trans, 99%), o-phenylenediamine (99.5%), trans-2-aminocyclohexanol hydrochloride (99%), 2-aminophenol (99%), cis-1,2-cyclohexanediol (99%), hexadecane (99%) were from Sigma-Aldrich; 25% ammonia water was from VWR chemical; sulfuric acid was from J. T. Baker; deuterium oxide (D, 99.9%) and deuterated DMSO (D, 99.9%) were from Cambridge Isotope Laboratories, Inc; deuterated ammonia water (25%, 99% D) was from Sigma-Aldrich.

Solvent: dichloromethane (99.8%), DMSO (99.9%), 1,4-dioxane (99.8%), 2-butanol (99.5%), hexane (95%), cyclohexane (99.5%) and dodecane (99%) were from Sigma-Aldrich; acetone (99.5%), tetrahydrofuran (HPLC, 99.9%), methanol (HPLC, 99.8%), ethanol (99.5%) and ethyl acetate (99.9%) were from VWR chemical; deionized water (DI water) was homemade using a purification system.

Catalyst: 10%Pd/C, 10%Pd/Al_2O_3, 10%Pd/$CaCO_3$, 5%Pd/$BaSO_4$, 1%Pd/Al_2O_3, 10%Pt/C, 10%Pt/graphitized carbon and 5%Pt/Al_2O_3 were from Sigma-Aldrich; 5%Ru/C was from Shaanxi Kaida Chemical engineering Co., Ltd.

Gas: hydrogen (99.9995%) and nitrogen (99.9995%) were from Air Liquide.

1.2 Experimental procedures

1.2.1 Reaction procedures in aqueous system

Typically, 5 ml DI water, 0.11 g (1 mmol) catechol, 30 mg 10%Pd/C, 0.5 ml 25% ammonia water (~7.4 mmol NH_3 molecule) and a glass-coated magnetic stir bar were added into a lining (10 ml) which was subsequently put into a reactor (total volume ~20 ml). The reactor was locked, then washed with hydrogen and pressurized with 0.5 MPa hydrogen (~3.3 mmol). Then, put the reactor into an oven which had been preheated to 220 °C and set magnetic stir speed to 400 rpm. Within 180 – 300 °C, the time for the temperature inside reactor reaching to target temperature is ~20 min. Thus, after 20 min, the reaction started and lasted for 1 h.

In the one-pot-two-step method, when the first step (as mentioned above) finished, tuning the temperature of the oven to 300 °C. The time for the temperature inside reactor and the oven reaching 300 °C from 220 °C is ~20 min too. Thus, after 20 min, the second step started and lasted for another 1 h.

When reaction finished, quench the reactor in flowing water to room temperature. Releasing the gas phase and took out the lining. There may be small amount (~0.5 ml) of liquid and crystal between lining and reactor wall due to evaporation and condensation in the reaction (always found when reaction temperature higher than

240 °C). If so, transfer this part into the lining and wash the lining and reactor with small amount of DI water (< 4 ml) and combine them together. The obtained mixture should be handled as soon as possible and better not to store for more than 4 h since catechol and other phenols are very easily oxidized under alkaline condition.

After that, the mixture was filtered using a small solvent filter (working volume 50 ml) and a 0.45 μm PTFE membrane. The lining and filter cake was washed with DI water (2 ml × 2 times) and the filtrate was combined. The filtrate was transferred to a bottle, weighted and extracted with dichloromethane (DCM, 2 ml × 3 times). The filter cake was dissolved with 2 ml acetone and filtered. Then, the lining and the filter cake were washed with acetone (2 ml × 2 times) and filtered. The acetone filtrate was transferred to a new bottle. The collector of the solvent filter was washed with additional 2 ml acetone. Then, all acetone and DCM phase were combined and evaporated. No need to completely evaporate all the solvent. The residual was redissolved with ~3 ml acetone (adding more acetone if not completely dissolved) and the internal standard (5% hexadecane in acetone) was added. The organic sample was ready for GC-FID or GC-MS. After extracted by DCM, the water phase was acidified using sulfuric acid to acidic condition. After filtrated using a 0.45 μm PES membrane, the water sample was ready for HPLC. By this method, all phenazine products were transferred into organic sample while catechol, 2-aminocyclohexanol, 2-aminophenol and majority of other impurities stayed in water sample.

1.2.2 Reaction procedures in organic system

The procedure is very similar to that in water system. But, typically, 1.5 or 2.5 MPa nitrogen gas was co-pressurized because of the low boiling point of some organic solvents and the function of nitrogen (Table S6). Besides, after reaction, a small amount (< 0.7 ml) of acetone was added to wash the lining and reactor wall, and transferred the solution into the lining. The combined mixture was filtered using a 0.45 μm PTFE syringe filter. In all reactions in organic solvent, the products were almost dissolved, so it was no need to analyze products in solid phase. The filtrate was added with internal standard solution and ready for GC. In the case of cyclohexane, the mixture was still biphasic even acetone and internal standard solution were added. Thus, the water phase was also detected by GC. It should be mentioned that the internal standard was completely absent in the water phase.

1.2.3 Analysis of phenazines using GC-FID and GC-MS

GC-FID conditions: Agilent 7890A with an FID and an automated injector; injector temperature: 300 °C; FID temperature: 310 °C; column: SGE BP5 (similar to HP-5) (15 m × 530 μm × 1.5 μm); column flow: 2 ml/min; oven temperature: 70 °C for 2 min, 15 °C/min to 300 °C, holding for 8 min.

The yield of **phzs** were calculated on mole bases. Since **phzs** are dimers of catechol, the yield of **phzs** is doubled.

$$\text{Yield of } \mathbf{phz}_i = (\text{mass of } \mathbf{phz}_i \,/\, \text{MW of } \mathbf{phz}_i) / 0.001 \times 2 \times 100\%$$

GC-MS conditions: Agilent 7890A-5759C with an automated injector; injector temperature: 300 °C; column: HP-5ms (30 m×250 μm×0.25 μm); column flow: 1 ml/min; oven temperature: 70 °C for 2 min, 15 °C/min to 300 °C, holding for 3 min.

It should be highlighted that catechol is unsuitable to be detected by GC because (1) the catechol peak is a severe tailing peak since the GC columns are non-polar; (2) major part of catechol was in the form of ammonium catechate which cannot be detected. And if it is acidified to catechol, the detection of **phzs** will be affected because they are basic so they form salt under acidic condition; (3) catechol may decompose in GC injector; (4) in cyclohexane system, **phzs** yield was high enough so catechol was almost consumed. Thus, we decided not to calculate catechol conversion for reactions in organic system.

1.2.4 Analysis of components in water phase using HPLC

HPLC conditions: Shimadzu LC-20A with a PDA and a RID; column: C18; mobile phase: 35%methanol-65%water, 0.4 ml/min; oven temperature: 40 °C.

Only samples from water system reactions were analyzed. The content of catechol and 2-aminophenol were calculated based on respective peaks under 254 nm while that of 2-aminocyclohexanol based on its peak under RID. Other peaks were not calculated due to low content.

Conversion = (1 - concentration of catechol × volume of sample / 0.11) × 100%;

Yield of 2-aminocyclohexanol or 2-aminophenol = (concentration of 2-aminocyclohexanol or 2-aminophenol × volume of sample) / MW of 2-aminocyclohexanol or 2-aminophenol / 0.001 × 100%;

where the concentration was determined by external standard method and the volume of sample was determined by the weight of the water filtrate described in 1.2.1 (the density was regarded as 1 g/ml since the content of the solute was low enough).

1.2.5 NMR detection for phenazine

The GC sample of 220+300 (Fig. 1(a)) was stored for weeks, so the solvent was gradually evaporated and **phz** was recrystallized to form needle-like crystal. The crystal was peaked out, dried and re-dissolved in d6-DMSO. The 1H NMR and 13C NMR spectra of the sample were detected using a Bruker Ascend 400 MHz NMR spectrometer. 13C NMR was operated in a fast mode.

1.2.6 Synthesis of hydrogenated phzs

The hydrogenated **phzs** were used to study dehydrogenation performance at different conditions. They were produced in cyclohexane system under the condition: cyclohexane 5 ml, catechol 1 mmol, 10%Pd/C 30 mg, 25% ammonia water 0.5 ml, H_2 0.5 MPa and N_2 2.5 MPa, 220 °C, 400 rpm and 1 h. After reaction the mixture was filtrated. The cyclohexane phase was extracted with diluted NaOH solution to remove small amounts of water-soluble components such as catechol and other impurities. Afterwards, the cyclohexane phase was evaporated to get the hydrogenated **phzs** solid.

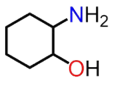
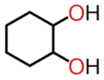
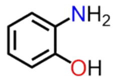
2. Results and discussion

Table S1. Performance of dehydrogenation over time at 0.5 or 1.0 MPa H_2 gas phase.[a]

Hydrogen pressure (Mpa)	Reaction conditions	Conversion (%)	Yield (%)			
			2-aminocyclohexanol	2-aminophenol	Total **phzs**	**phz** purity
0.5	First step	89.5	9.3	0	66.8	0
	300 °C, 10 min	91.2	5.7	0.7	69.6	84.3
	300 °C, 20 min	89.3	4	0.8	68.3	91.1
	300 °C, 40 min	88.4	4.2	0.8	61	95.4
1	First step	95	15.7	0	61.2	0
	300 °C, 10 min	96.5	8.7	1.2	71.9	60
	300 °C, 20 min	97.9	7	1.3	69.4	71.3
	300 °C, 40 min	97.1	5.8	1.3	69.4	56.3

[a] Reaction conditions: the first step: water 5 ml, catechol 1 mmol, 10%Pd/C 30 mg, 25% ammonia water 0.5 ml, H_2 0.5 or 1.0 MPa, 220 °C, 400 rpm and 20 min; the second step: after the first step, increase temperature to 300 °C and continue for 10 – 40 min.

Table S2. Conversion of intermediates.[a]

Substrate	Conditions	Total phzs yield (%)
	$\xrightarrow[\text{ammonia water}]{\text{220 °C, Pd/C}}$	9.6 (13.3)
	$\xrightarrow[\text{ammonia water}]{\text{300 °C, Pd/C}}$	18.4 (72.9)
	$\xrightarrow[\text{ammonia water}]{\text{220 °C, Pd/C}}$	1.1 (13.8)
	$\xrightarrow{\text{300 °C, Pd/C}}$	11.1

[a] Reaction condition: water 5 ml, substrate 1 or 0.5 mmol, 10%Pd/C 30 mg, 25% ammonia water 0.5 ml (if applicable), H_2 0.5 MPa, 220 or 300 °C, 400 rpm and 1 h. The numbers in parathesis indicate the conversion.

Discussion for Table S2: Three intermediates were tested for reactivity. 2-aminocyclohexanol showed certain activity to form **phzs**. So, 2-aminocyclohexanol is a minor source of **phzs**. Note that the conversion at 300 °C was high. In factor, in this case, ~6% of 2-aminophenol and ~6% catechol were formed while majority part (~40%) is undetected. Thus, we consider 2-aminocyclohexanol is the major source to generate undetectable products, probably being oligomers. And the conversion of 2-aminocyclohexanol is probably triggered by the dehydrogenation activity of Pd/C so the conversion become higher at high temperature.

Table S3. Stability of chemicals in water and cyclohexane phases.[a]

Substrate	Recovery (%) Water phase	 cyclohexane phase
8H-phz	39.4[b]	93.7
phz	84.2	98.4
propylguaiacol	55.4	90.2
n-hexadecane	60	98.3

[a] Reaction conditions: water or cyclohexane 5 ml, substrate 60 – 130 mg, N_2 0.5 MPa, 220 °C, 400 rpm and 1 h. [b] 300 °C was used instead of 220 °C.

Description and discussion for Table S3: The purpose of this part is to find if chemicals are stable in the reaction or not. The chemicals were placed in the solvent and heated to 220 or 300 °C under N_2 gas. As shown in Table S3, after reaction, more than 90% of the chemical can be found in cyclohexane phase, indicating the chemicals were not significantly decomposed or changed in cyclohexane system. However, in water system, large part of the chemicals was lost. This is believed to be the hydrolysis. Hydrothermal condition is known to break down linkages such as ether bond and C-C bond. And such a condition is one of method to depolymerizing lignin[1]. We believe the hydrolysis effect contributed to the formation of undetectable products.

Table S4. Catalysts screen in water system.[a]

Catalyst	Conv. (%)	Yield (mol%) **2-aminocyclohexanol**	**14H-phz**	**8H-phz**	**8H-phz 2**	**4H-phz**	**phz**	total **phzs**
10%Pd/C	98.2	12.3	14.7	48.1	0.9	0.4	0	64.1
10%Pd/Al_2O_3	90.7	9.4	17.9	40.7	1.4	0.5	0	60.6
10%Pd/$CaCO_3$	85.1	4.0	6.7	53.5	0.6	0.0	0	60.8
5%Pd/$BaSO_4$	60.2	0.9	2.4	40.6	0.3	0.3	0	43.6
1%Pd/Al_2O_3	42.9	2.7	11.0	25.1	0	0.4	0	36.5
10%Pt/C	100.0	1.1	0.2	38.8	0.5	1.1	0.2	41.0
10%Pt/graphitized carbon	100.0	2.4	0.3	30.6	1.2	0.6	0	32.8
5%Pt/Al_2O_3	93.6	17.7	10.4	26.4	2.7	0.9	0	40.8
5%Ru/C	28.3	1.5	0	1.2	0	0	0	1.2

[a] Reaction condition: water 5 ml, catechol 1 mmol, catalyst 30 mg, 25% ammonia water 0.5 ml, H_2 0.5 MPa, 220 °C, 400 rpm and 1 h.

Table S5. Study of internal diffusion by using grinded catalysts in water system.[a]

Catalyst	Size	Conversion (%)	Yield (mol%)	
			2-aminocyclohexanol	Total **phzs**
10%Pd/C	As purchased	98.2	12.3	64.1
	Mild grinded	95.5	11.0	64.9
	Hard grinded	93.5	10.1	67.5
10%Pd/Al_2O_3	As purchased	90.7	9.4	65.5
	Mild grinded	87.7	8.0	66.3
	Hard grinded	79.2	6.2	63.7

[a] Reaction condition: water 5 ml, catechol 1 mmol, catalyst 30 mg, 25% ammonia water 0.5 ml, H_2 0.5 MPa, 220 °C, 400 rpm and 1 h. The catalysts were grinded by using an agate mortar. Mild grinded: grinded for ~5 min; Deep grinded: grinded for another ~5 min. Although the actual particle sizes were not measured, based on our experiences, mild grinded samples are fine enough to serve as XRD samples; while deep grinded samples are fine enough to serve as TEM samples.

Table S6. Dehydrogenation of hydrogenated **phz** under different gas phases.[a]

Gas phase	**phzs** distribution (%)			Total yield (%)
	8H-phz (including **8H-phz 2**)	**4H-phz**	**phz**	
2.5 MPa N_2	18.2	39.9	41.9	82.0
0.5 MPa N_2	1.9	16.7	81.4	89.5
0.5 MPa N_2, 0.5 h	6.1	3.9	90.0	87.5
0.5 MPa H_2 + 0.5 ml 25% ammonia water	2.6	3.2	94.2	92.7
0.5 MPa H_2	0.0	0.9	99.1	90.3
0.5 MPa H_2, 0.5 h	5.5	2.8	91.8	89.8
0.5 MPa H_2+2.5 MPa N_2	94.7	5.3	0.0	49.0
0.5 MPa N_2 without catalyst	86.9	9.9	3.2	39.4
0.5 MPa H_2, cyclohexane, 280 °C	72.7	24.7	2.7	96.1
0.5 MPa N_2, cyclohexane, 280 °C	30.3	55.4	14.3	90.9

[a] Reaction condition: water 5 ml, hydrogenated **phzs** 0.35 mmol, 10%Pd/C 30 mg, 300 °C, 400 rpm and 1 h (if not specified).

Discussion for Table S6: The results in this Table show dehydrogenation performances in water and the function of N_2 in the dehydrogenation. With N_2, dehydrogenation was unable to complete. This is due to the formation of the mixture of N_2 and H_2 (released from hydrogenated **phzs**) and the combination of the two gas obviously increases hydrogenation ability and suppresses dehydrogenation ability. The detailed mechanism is unclear but is considered not related to deactivation of catalyst since adding ammonia water did not evidently decrease yield and selectivity of **phz**. As shown in this Table, only low pressure H_2 can be the working gas phase in the dehydrogenation reaction. 90.3% of yield with GC purity of 99.1% were obtained. The purity is higher than one-pot-two-step method because the composition of products was not affected by other impurities such as catechol and 2-aminocyclohexanol. When N_2 and H_2 were co-pressurized or the catalyst was not used, the yield was strongly decreased. The decrease of yield is believed due to hydrolysis (Table S5), and that is probably the reason for the ~10% loss of **phzs** for other samples. The results indicate that Pd/C helped to retain **phzs** but the mechanism is also unclear. Again, dehydrogenation in cyclohexane phase is far from complete.

Table S7 Effect of temperature on the conversion of catechol in biphasic cyclohexane-aqueous ammonia system.[a]

Temperature (°C)	Yield (mol%)			
	14H-phz	**8H-phz**	Other **phzs**	Total **phzs**
220	31.1	57.0	1.4	89.5
190	42.7	43.6	0.9	87.2
150	32.4	41.7	2.8	76.9
120	12.5	12.8	1.3	26.6
120 (4h)	32.1	27.1	2.8	62.0

[a] Reaction conditions: cyclohexane 5 ml, catechol 1 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa + N_2 2.5 MPa, 25% ammonia water 0.5 ml, 400 rpm and 1 h or specified time.

Table S8. Comparison of ways of adding ammonia water.[a]

Adding ways	Yield (mol%)			
	14H-phz	**8H-phz**	Other **phzs**	Total **phzs**
0.5 ml, added normally	0	66.4	8.3	74.7
0.5 ml, added outside lining	0	38.7	6.2	44.9
1.0 ml, added outside lining	0	47.8	6.5	54.3

[a] Reaction conditions: cyclohexane 5 ml, catechol 1 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa, 25% ammonia water 0.5 or 1.0 ml, 220 °C, 400 rpm and 1 h. As indicated in Adding ways column, ammonia water was added normally (i.e., added together with cyclohexane phase) or outside lining (i.e., between the lining and the reactor wall).

Discussion for Table S8: By adding outside lining, water is unable to directly contact with the cyclohexane phase. In fact, no matter which way was used, ammonia molecule is almost released into the gas phase due to the high temperature during the reaction. So, the differences of the yield were not from ammonia aspect.

The reason for not using ammonia gas is as follow: based on calculation, if ammonia gas was used, ~ 1 MPa ammonia gas would be needed for providing the same amount of ammonia in 0.5 ml 25% ammonia water. Such a high pressure of ammonia was considered not safe in our lab. And the co-pressure of H_2 increase the degree of difficulty and danger. So, we decided to add ammonia water outside lining to stimulate the condition of without water.

Table S9. Attempts to produce **phz** in organic solvents.

Method	Solvent	Temperature (°C)	Yield (%)				
			14H-phz	**8H-phz** (include **8H-phz 2**)	**4H-phz**	**phz**	Total
One-pot-two-step[a]	CH	220	31.1	58	0.4	0	89.5
	CH	220+260	1.4	84.7	0.9	0	86.9
	CH[c]	220+280	0	39.3	30.9	6.6	76.8
	n-dodecane	220+300	0	65.2	2.5	0	67.7
Conversion of hydrogenated **phzs**[b]	CH[c]	280	0	69.8	23.8	2.6	96.2
	CH[d]	280	0	27.5	50.4	12.9	90.8
	n-dodecane[c]	300	1.6	78.3	1.8	0	81.7
	Toluene[e]	300	0	17.7	52.8	24.7	95.2

[a] Reaction conditions: first step: solvent 5 ml, catechol 1 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa and N_2 2.5 MPa, 25% ammonia water 0.5 or 1.0 ml, 220 °C, 400 rpm and 1 h; second step: after first step, increase temperature to designated value and continue another 1h; [b] Reaction conditions: solvent 5 ml, hydrogenated **phzs** 0.35 mmol, 10%Pd/C 30 mg, 400 rpm and 1 h; [c] In these cases, the pressure were H_2 0.5 MPa; [d] In this case, the pressure was N_2 0.5 MPa; [e] The pressure was N_2 3 MPa and reaction time was 0.5 h.

Table S10. Mass increase of chemicals in isotope exchange experiment.[a]

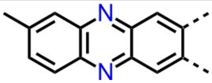
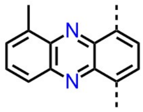
Conditions	Average molecular weight increment (g/mol)					
	catechol	2-hydroxyl-cyclohexanone	1,2-cyclohexanediol	2-amino-cyclohexanol	**14H-phz**	**8H-phz**
D_2O+H_2-120 °C	1.0	5.2	6.3	Not detected (n.d.)		
D_2O+H_2-180 °C	1.8	6.6	7.3			
D_2O+ND_3+H_2-180 °C	3.2	8.1	n.d.	8.5	16.6	6.9
D_2O+ND_3+H_2-180 °C-80min	4.3	n.d.	n.d.	8.9	17.0	7.9

[a] Reaction conditions: Deuterated water 5 ml, catechol 1 mmol, 10%Pd/C 30 mg, 25% fully deuterated ammonia water 0.5 ml if indicated with ND_3, H_2 0.5 MPa, 120 or 180 °C, 400 rpm, 25 or 80 min (starting from putting reactor into oven).

Description and discussion for Table S10: the conversion of catechol to **phzs** were tested using deuterated reagents to study the mechanism. After reactions, all chemicals were deuterated to certain extend because deuterated reagents (i.e., D_2O and ND_3) were involved in the conversion. Thus, the mass (molecular weight, MW) of a chemical increased and was detected with GC-MS. By solving the percentage of peak area of each isotope isomers in GC, we can calculate the increment of average molecular weight of a component. For example, the first value, 1.0, for entry 1 and catechol, indicates that in this sample, on average, catechol has 1.0 (of 6) hydrogen exchanged to deuterium.

The results show that in hydrogenation reaction (entry 1 and 2), catechol was hydrogenated with deuterium instead of H atom. This means D_2O involved in the reaction and D in D_2O were transferred to catechol. While in amination reaction (entry 3 and 4) we found **14H-phz** had ~17 (of 22) hydrogen deuterated. Such lots of D mainly came from H/D exchange during hydrogenation and amination. However, in **8H-phz**, only 7-8 (of 16) D were found. The difference of D number in **14H-phz** and **8H-phz** was more than 9. Thus, it must be that **8H-phz** formed followed by hydrogenation to **14H-phz** and during the hydrogenation more H were deuterated. It is not vise versa because D in **14H-phz** is not possible to be changed back to H under the conditions and at most 6 D can be removed.

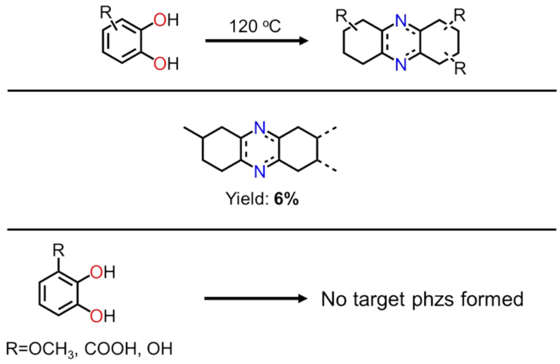
Table S11 Dehydrogenation of alkylated hydrogenated **phzs** for alkylated **phz**.[a]

Alkylated **phz**	Time (h)	Total **phzs** yield (%)	**phz** purity (%)
	0.5	58.5	67.8
	1	59.3	74.9
	0.5	35.4	76.7
	1	32.4	73.1

[a] Reaction condition: water 5 ml, alkylated hydrogenated (rich in **14H-** and **8H-**) **phzs** 0.35 mmol, 10%Pd/C 30 mg, 300 °C, 400 rpm and 0.5 or 1 h.

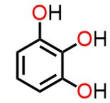
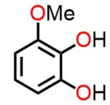
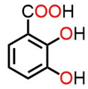
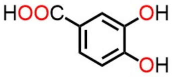
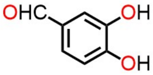
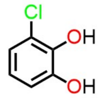
Table S12. Amination and hydrogenation of substituted catechols under low temperature.

Table S12-1. Amination of substituted catechols at 120 °C.[a]



[a] Reaction condition: cyclohexane 5 ml, substituted catechol 1 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa and N_2 2.5 MPa, 25% ammonia water 0.5 ml, 120 °C, 400 rpm and 1 h.

Table S12-2. Hydrogenation of substituted catechols at 50 or 80 °C.

	Water, 50 °C[a]	Ethyl acetate, 80 °C[b]			Cyclohexane, 80 °C[c]
Catechols substrate	2-Hydroxyl-cyclohexanone yield (%)	Conversion (%)	2-Hydroxyl-cyclohexanone yield (%)	Other major product yield (%)	2-Hydroxyl-cyclohexanone yield (%)
	44	23	13	-	5
	23	3	3	-	2
	10	13	0	-	2
	0	3	0	-	-
	0	100	5	90 (4-methyl-catechol)	0
	0	72	12	43 (catechol)	-

[a] Reaction condition: water 5 ml, substituted catechol 0.5 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa and N_2 2.5 MPa, 50 °C, 400 rpm and 1 h; [b] Reaction condition: ethyl acetate 5 ml, substituted catechol 0.5 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa and N_2 2.5 MPa, 80 °C, 400 rpm and 1 h; after reaction, the product mixtures were derivatized using BSTFA, so catechols were properly detected and conversion were calculated. [c] Reaction condition: cyclohexane 5 ml, substituted catechol 1 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa and N_2 2.5 MPa, 80 °C, 400 rpm and 1 h.

Discussion for Table S12: In this part, more tests were done to find out why substituted catechols are unable to be transformed to corresponding **phzs**. In fact, in most reactions at 220 °C using catechols with non-hydrocarbonic group, unsubstituted **phzs** or methyl-**phzs** were formed with low yield (<15%), which indicated the substituted groups were destroyed or reduced to methyl group. In Table S12-1, we conducted the reaction at 120 °C which is low enough to avoid possibly thermal pyrolysis. Still, no target **phzs** were found. Then, in Table S12-2, we tried to hydrogenate the catechols at even 50 or 80 °C in water, ethyl acetate and cyclohexane since hydrogenation, based on the mechanism (Scheme 1), is the first step of the reaction. We unexpectedly found the substituted groups were also disappeared and unsubstituted 2-hydroxyl-cyclohexanone were formed as the major product in most cases. Carbonyl was quickly reduced to methyl. Considerable products are undetectable by GC and GC-MS, probably due to polymerization since catechols are reactive. The results above explain why no target substituted **phzs** was formed in amination reactions at 220 °C (Table 2). However, the hydrogenation mechanism is unclear at present stage. And we don’t find literatures report hydrogenation functionalized catechol to corresponding 2-hydroxyl-cyclohexanone.

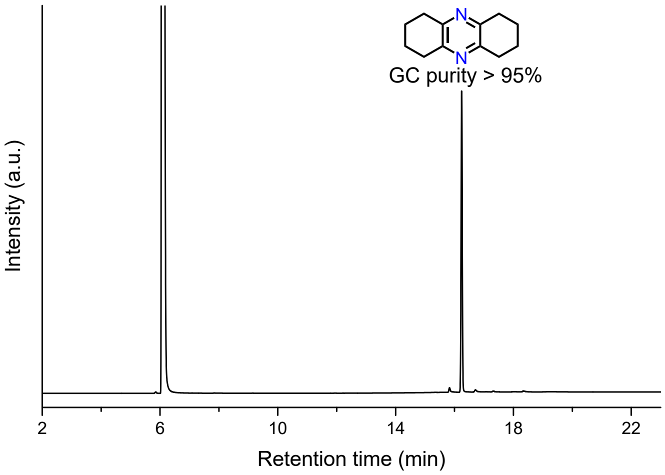


Fig. S1. GC spectrum of crystal product from the following conditions: water 5 ml, catechol 1 mmol, 10%Pd/C 30 mg, H_2 0.5 MPa, 220 °C, 400 rpm and 1 h; After reaction, the solid was filtered and washed with water (1 ml × 2 times). Then, the crystal was dissolved, filtered from the catalyst and detected.

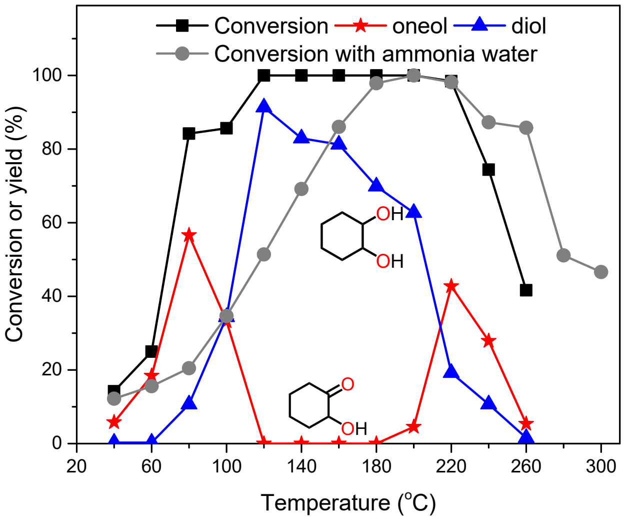


Fig. S2. Hydrogenation of catechol over temperature. The conversion of catechol with ammonia water (also presented in Fig. 1a) is presented for comparison.

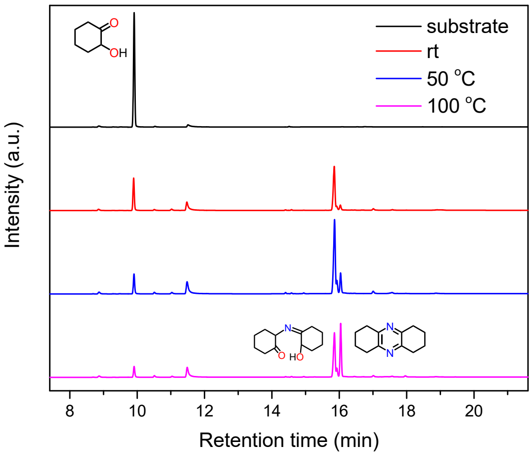


Fig. S3. GC spectra of conversion of 2-hydroxyl-cyclohexanone with ammonia at low temperature. Reaction condition: water solution of 2-hydroxyl-cyclohexanone 2 ml, 25% ammonia water 0.1 ml, 15 min at designated temperature.

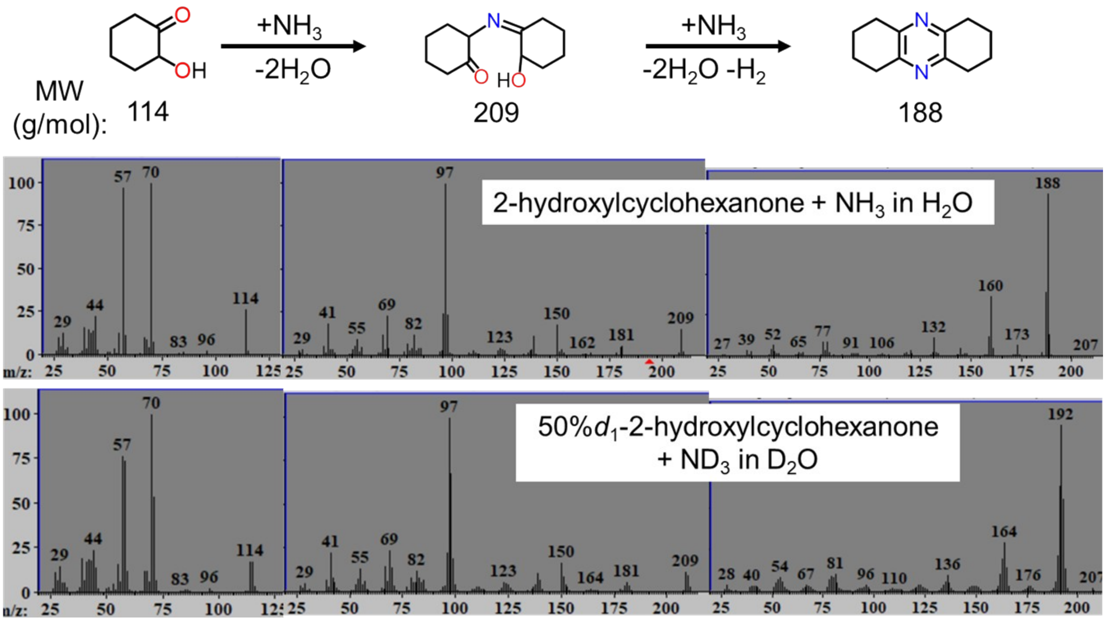


Fig. S4. MS spectra of 3 chemicals in GC-MS for the reactions of 2-hydroxyl-cyclohexanone with normal ammonia water or fully deuterated ammonia water. Reaction condition: for reaction with normal ammonia water: water solution of 2-hydroxyl-cyclohexanone 2 ml, 25% ammonia water 0.1 ml, 500 rpm, 15 min; for reaction with deuterated ammonia water: the water solution of 2-hydroxyl-cyclohexanone was extracted with dichloromethane, followed by evaporation and redissolving in deuterated water. The solution was added with fully deuterated 25% ammonia water 0.1 ml, and reacting for 15 min.

Discussion for Fig.S4: The reaction of ketones and ammonia molecule has turned out to be very easy to form imines at even room temperature[2, 3]. Thus, it is believed that 2-hydroxyl-cyclohexylimine is the product of 2-hydroxyl-cyclohexanone and ammonia molecule. And this isotope exchange experiment is used to help identify how 2-hydroxyl-cyclohexylimine is converted to **pre-phz**.

In the normal conversion, **pre-phz** was detected with MW of 209 g/mol which subsequently form **8H-phz** (Fig. S3). In order to perform the deuterated experiment, we extracted 2-hydroxyl-cyclohexanone and redissolved it in deuterated water. During the process, we found ~50% 2-hydroxyl-cyclohexanone was deuterated with 1 deuterium atom, as the intensity of 115 was equal with 114 in the MS spectra. And the position of this deuterium atom should mainly be the H in hydroxyl group since the group is more active. In the MS spectrum of **pre-phz** in deuterated sample, we found the signal of 210 was close to 209 while 211 had certain intensity. The results also indicated that ~50% **pre-phz** had 1 H atom deuterated. By forming **pre-phz**, 2 2-hydroxyl-cyclohexanone and 1 NH_3 are reacted while releasing 2 H_2O, which means 3 H were added while 4 H were released. Therefore, combining the MS results, in the deuteration experiment, 3 D in ND_3 molecule and 1 H/D in 2-hydroxyl-cyclohexanone were removed in the form of 1 D_2O and 1 H/D-O-D. We don't find any strong evidence that support that imido group can react with hydroxyl. Thus, the only explanation for the conversion is that the H/D in the hydroxyl in 2-hydroxyl-cyclohexylimine is transferred to the N atom to a form amino group which subsequently reacts with the carbonyl of another 2-hydroxyl-cyclohexanone and form **pre-phz**.

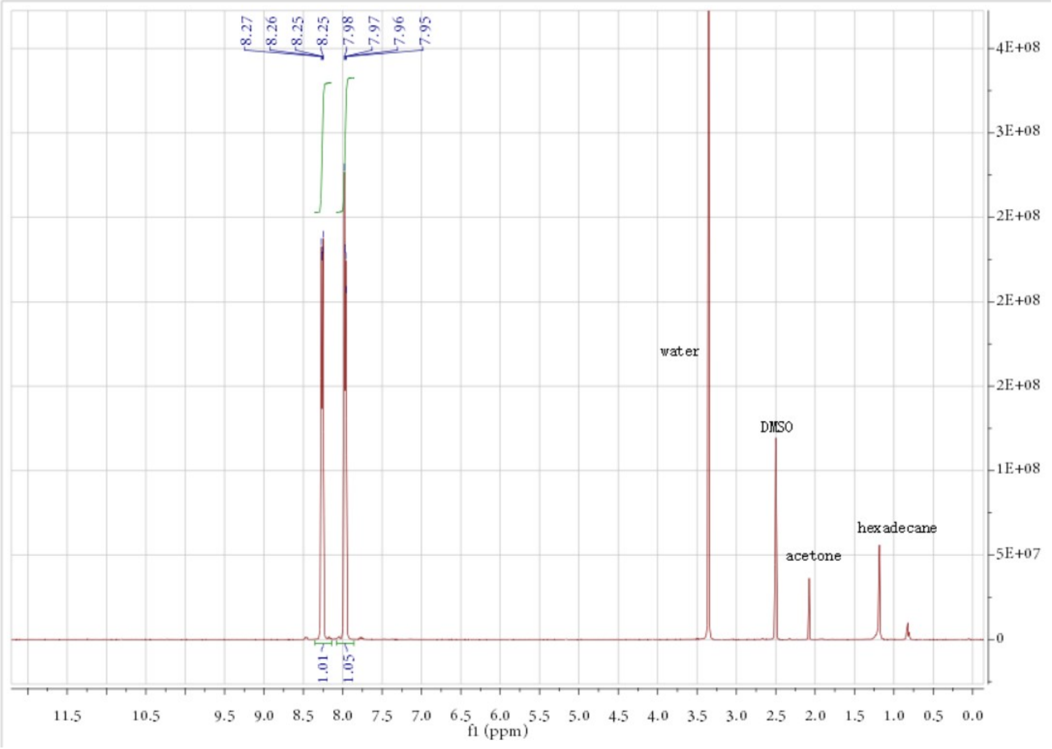


Fig. S5-1 1H NMR of **phz** crystal. Note: the sample came from recrystallization of **phz** in GC sample, so it contained impurities which doesn't affect the identification of **phz**. The peaks of **phz** are same with those reported in literatures[4, 5].

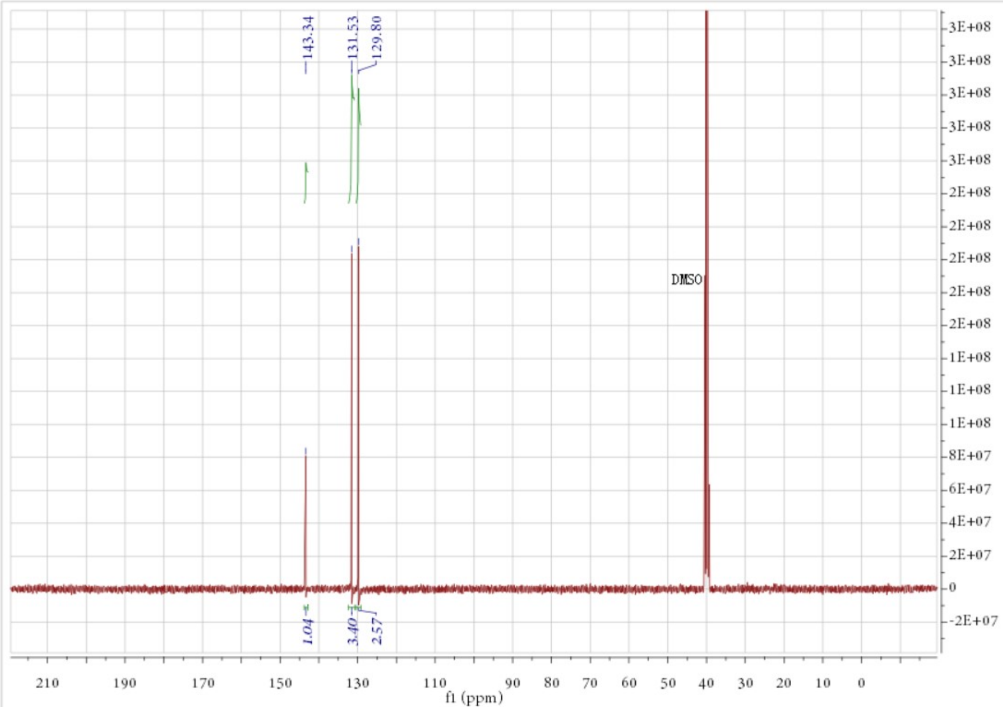


Fig. S5-2 13C NMR of **phz** crystal. The peaks of **phz** are same with those reported in literatures[4, 5].

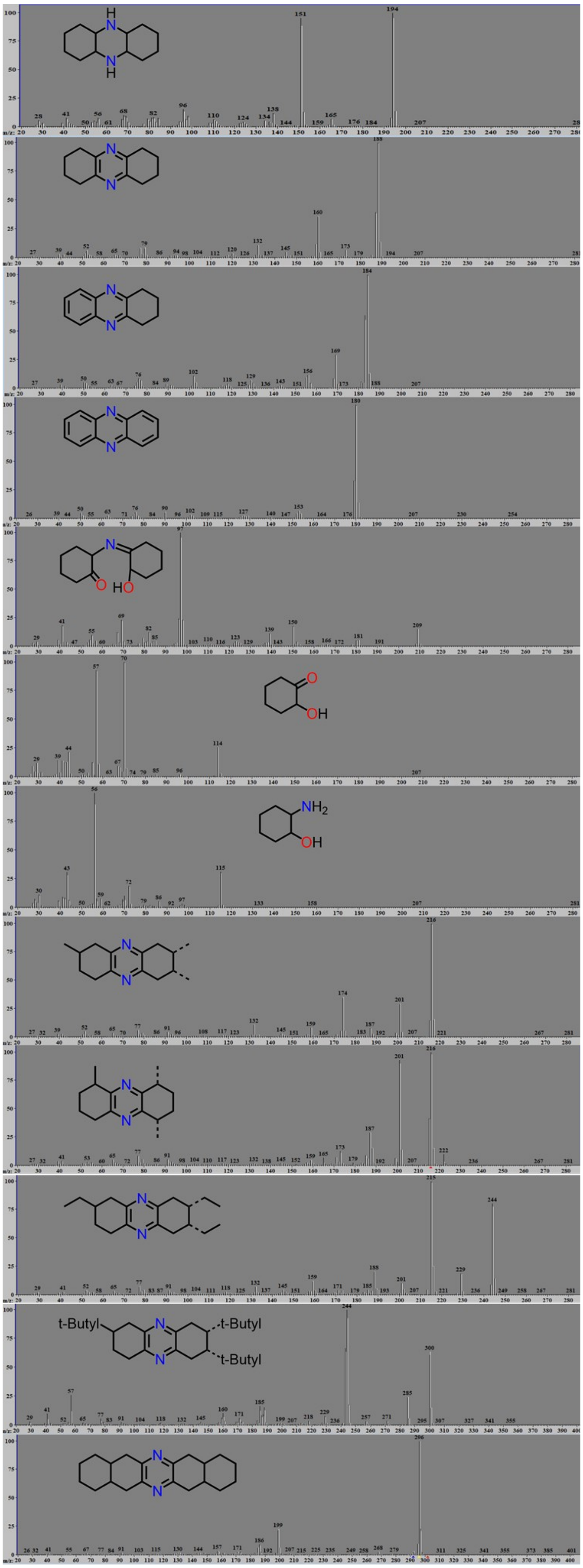
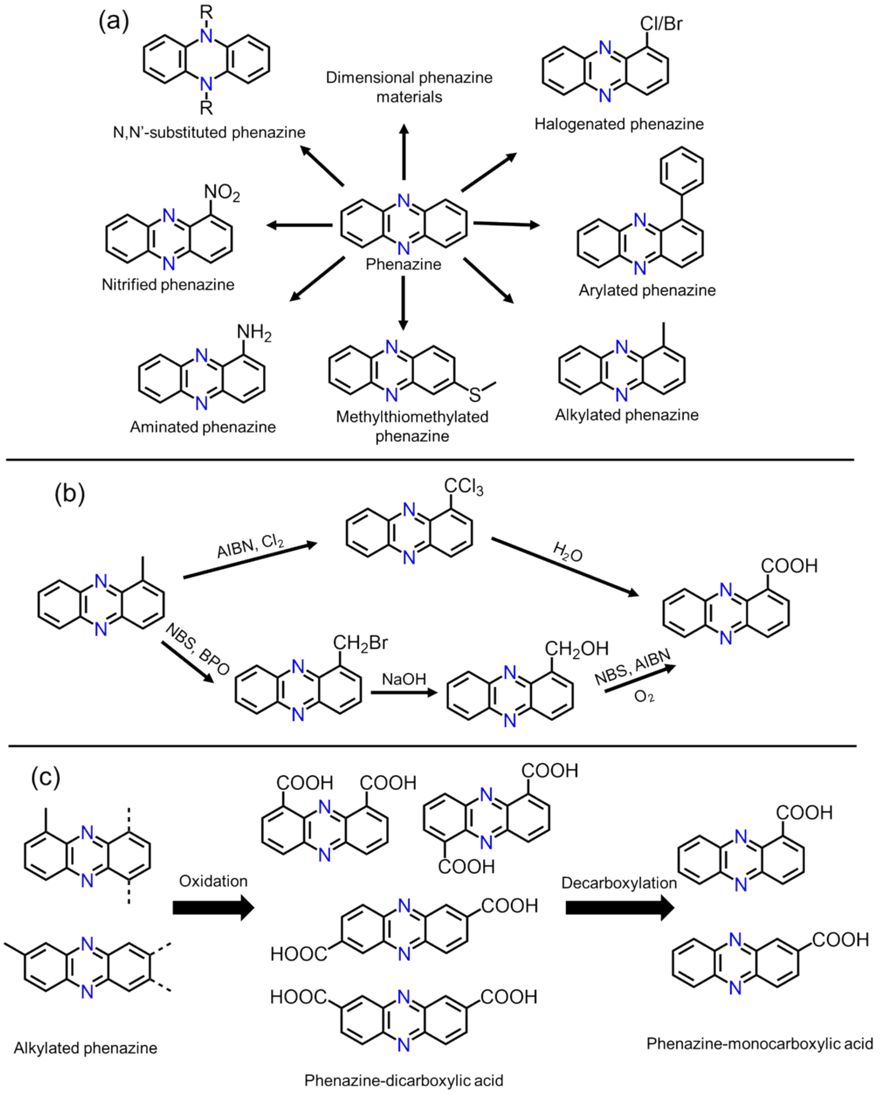


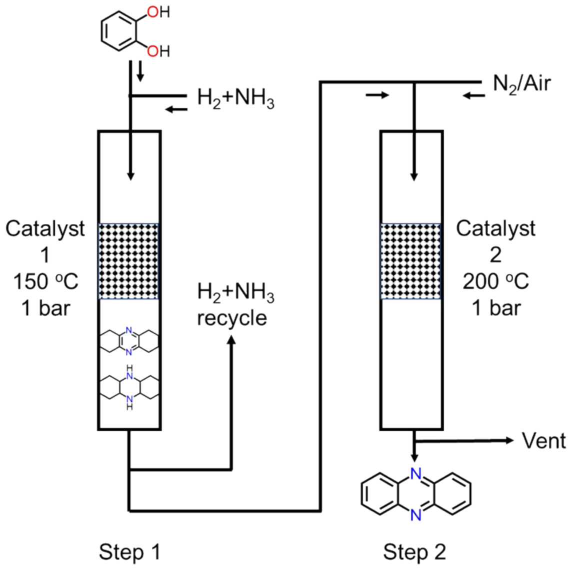
Fig. S6. MS spectra of main **phzs** and intermediates in GC-MS.



Scheme S1. Functionalized **phzs** produced from **phz** and alkylated **phz**. (a) functionalization (including N,N'-substitution,[6-8] halogenation,[8] nitration,[4] arylation,[9] amination,[8] methylthiomethylation,[10] alkylation,[11] etc.) of **phz**; (b) pathway of oxidation of methyl to produce carboxylic **phz** (abbreviation: AIBN: azobisisobutyronitrile; NBS: N-bromosuccinimide; BPO: dibenzoyl peroxide);[12, 13] (c) possible valuable carboxylic **phzs** oxidized from alkylated **phzs**.

Discussion for Scheme S1: This Scheme shows the generality of phenazine-derived products that can be synthesized from **phz** and alkylated **phzs**. Due to the reactivity of N atoms, **phz** is readily to produce N- (or N,N'-) substituted derivatives and macromolecules, many of which are of current research and application interests. For example, 5,10-dihydro-5,10-dimethylphenazine was used as cathode material of organic battery and showed high voltage (>3V vs. Li/Li+) and high energy density (622 Wh/kg);[7] and a redox-active supramolecular capsule with 1 nm size was synthesized from **phz** via N'N-substitution.[14] Other functionalization methods demonstrate that diversified functionalized **phzs** are available from **phz**.

The production of carboxylic **phzs** (Scheme S1(a) and (b)) is highlighted as many carboxylic **phzs** are widely studied thanks to their antibiotic function. For example, phenazine-1-carboxylic acid (the product in Scheme S1(b)) is a commercial agricultural fungicide widely applied in China.[15] Phenazine-1,6-dicarboxylic acid showed excellent antibiotic and anticancer activity.[16] Apart from that, many carboxylic **phzs** have been used as organic cathode material and showed energy density higher than 400 Wh/kg.[17] Carboxyl was found to help increase redox potential of the **phzs**. Therefore, by applying the current functionalization (Scheme S1(a)) and oxidation protocols (Scheme S1(b)),[12, 13] many valuable functionalized **phzs** can be produced from **phz** and alkylated **phzs** which are available from the pathway presented in this work.



Scheme S2. A design of reactor set-up that could be operated at mild conditions.

Discussion for Scheme S2: A flow reaction can work milder than a batch one because, in flow mode, vapor pressure of solvent and substrates do not contribute to the reaction pressure, so an ambient pressure system can be established; and hydrogen formed in step 2 can be quickly removed, so dehydrogenation can be promoted. In this design, we estimate that 150 °C will be enough for the formation of hydrogenated **phzs** (step 1) based on our findings (e.g., Fig. S2 and S3). Pressure of the gas is not necessary as this step is fast. For the step 2 (dehydrogenation), we estimate 200 °C may be enough based on our experience and by comparing with other works.[18, 19] Moreover, air (if possible) could be added to help dehydrogenation and lower the temperature.[20] It should be noted that the melt point of **phz** is ~170 °C (while that of the product of step 1 was found lower than 100 °C). So, the temperature of step 2 must be higher to avoid crystallization and block the reactor.

3. Reference

1. S. Kang, X. Li, J. Fan and J. Chang, *Renewable Sustainable Energy Rev.*, 2013, **27**, 546-558.
2. C. Xie, J. Song, M. Hua, Y. Hu, X. Huang, H. Wu, G. Yang and B. Han, *ACS Catal.*, 2020, **10**, 7763-7772.
3. S. Song, Y. Wang and N. Yan, *Mol. Catal.*, 2018, **454**, 87-93.

4. Y. Xiao, X. Wu, H. Wang, S. Sun, J. T. Yu and J. Cheng, *Org Lett*, 2019, **21**, 2565-2568.
5. L. Yu, X. Zhou, D. Wu and H. Xiang, *Journal of Organometallic Chemistry*, 2012, **705**, 75-78.
6. P. Veerakumar, S. Balakumar, M. Velayudham, K.-L. Lu and S. Rajagopal, *Catalysis Science & Technology*, 2012, **2**.
7. M. Lee, J. Hong, B. Lee, K. Ku, S. Lee, C. B. Park and K. Kang, *Green Chemistry*, 2017, **19**, 2980-2985.
8. U. Urleb and S. Gobec, in *Science of Sythesis*, eds. Y. Yamamoto and I. Shinkai, Thieme, 2004, ch. Product class 16: phenazines, pp. 913-943.
9. J. Kwak, M. Kim and S. Chang, *J Am Chem Soc*, 2011, **133**, 3780-3783.
10. R. A. Garza-Sanchez, T. Patra, A. Tlahuext-Aca, F. Strieth-Kalthoff and F. Glorius, *Chemistry*, 2018, DOI: 10.1002/chem.201802352.
11. *CN Pat.,* 107954943 A, 2016.
12. *CN Pat.,* 103304496 A 2012.
13. *CN Pat.,* 104045601 A 2014.
14. K. Yazaki, S. Noda, Y. Tanaka, Y. Sei, M. Akita and M. Yoshizawa, *Angew Chem Int Ed Engl*, 2016, **55**, 15031-15034.
15. L. Ye, H. Zhang, H. Xu, Q. Zou, C. Cheng, D. Dong, Y. Xu and R. Li, *Bioorg Med Chem Lett*, 2010, **20**, 7369-7371.
16. M. Bilal, S. Guo, H. M. N. Iqbal, H. Hu, W. Wang and X. Zhang, *World Journal of Microbiology and Biotechnology*, 2017, **33**.
17. L. Miao, L. Liu, K. Zhang and J. Chen, *ChemSusChem*, 2020, **13**, 2337-2344.
18. Z. Wei, F. Shao and J. Wang, *Chin. J. Catal.*, 2019, **40**, 980-1002.
19. Y. Sekine and T. Higo, *Topics in Catalysis*, 2021, **64**, 470-480.
20. J. H. Carter, T. Bere, J. R. Pitchers, D. G. Hewes, B. D. Vandegehuchte, C. J. Kiely, S. H. Taylor and G. J. Hutchings, *Green Chemistry*, 2021, DOI: 10.1039/d1gc03700e.