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ARTICLE

Direct production of indoles via thermo-catalytic conversion of bio-derived furans with ammonia over zeolites

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In this study we demonstrate that indoles can be directly produced by thermo-catalytic conversion of bio-derived furans with ammonia over zeolite catalysts. MCM-41, β -zeolite, ZSM-5 (Si/Al=50) and HZSM-5 catalysts with different Si/Al ratios (Si/Al=25, 50, 63, 80) were screened and HZSM-5 with Si/Al ratio as 25 showed best reactivity for indoles production due to the desired pore structure and acidity. Temperature displayed significant effect on the product distribution. The maximum yield of indoles was obtained at moderate temperatures around 500 °C. The weight hourly space velocity (WHSV) of furan to catalyst investigation indicated that a lower WHSV could cause the overreaction of furan over the catalyst to produce more aniline and pyridines, while a higher WHSV would cause the incomplete reaction of furan. Because ammonia served as both reactant and carrier gas, to supply sufficient reactant and keep desired reaction time, appropriate ammonia to furan molar ratio was important on furan conversion to indoles. Under the optimized conditions, the highest total carbon yield of indoles and their selectivity in the N-containing chemicals were 32% and 75%, respectively. 2-Methylfuran and the mixture of furan and 2-methylfuran were also studied, which demonstrated that more alkyl indoles could be selectively obtained via coupling reaction of different bio-derived furans. Ring opening of the furan is a more favorable mechanism compared to Diels-alder mechanism, and the pyrrole reacting with furan is the more favorable pathway compared to pyrrole reacting with pyrrole based on our experimental and theoretical calculations.

Introduction

Indoles, one of the most abundant and important classes of heterocycles in nature, have found wide applications as pharmaceuticals, agricultural chemicals, dyes, and other functional materials.¹ Since indole was isolated by von Baeyer in 1866, the synthesis and functionalization of indoles has been a major focus for synthetic organic chemists, and a wide array of approaches have been developed.² For example, the first practical and important indole synthesis method was based on the cyclization of an arylhydrazone using an acidic treatment proposed by Fischer and Jourdan in 1883.³ The Möhlau – Bischler synthesis demonstrated that excess of aniline with *o*-bromoacetophenone was also a route to 2-arylated indoles.⁴ The first carbazole synthesis by thermal decomposition of triazole was reported by Graebe and Ullmann.⁵ Other well-known methods for indole synthesis are as namely Madelung's intramolecular synthesis, Nenitzescu's synthesis, Batcho-Leimgruber's reaction, Gassman's reaction, and Bartoli's synthesis, etc.⁶ Despite great advances, most of these methods

rely heavily on reactant pre-synthesis or pre-activation.^{1e, 2a} The starting material scarcity and sometimes combined with toxicity which always results in the multiple complicated synthesis steps and environmental problems have been the restrictive issues for the large-scale preparation of indoles.^{2a,c,d,g} Therefore, developing practical, safe, and scalable methods by using abundant and environment friendly starting materials for the indoles production is of critical interest to the researchers both in academia and in industry.

Biomass, abundant and inexpensive, has been regarded as the only renewable source of organic carbon for the production of renewable fuels and commodity chemicals.⁷ Biomass-derived furans, such as furan (FR), 2-methylfuran (2-MF), are important platform molecules that can be produced from biomass by pyrolysis, hydrolysis, and subsequent dehydration of hemicellulose and cellulose.⁸ Because biomass-derived furans are generally considered as pyrolysis intermediates in the catalytic fast pyrolysis of biomass, recently, many studies on conversion of biomass-derived furans to aromatics (benzene,

toluene and xylenes) via catalytic fast pyrolysis (CFP) process were performed.⁹ Through this process, Chen et al. successfully converted furan and even biomass to aromatics and p-xylene over ZSM-5 and modified ZSM-5 catalysts.¹⁰ The chemistry of this process was investigated and it was found that benzofuran was an important intermediate.^{10d} Vaitheeswaran et al. further performed kinetics experiments and utilized theoretical methods to investigate the mechanism for conversion of furan to benzofuran.¹¹ Because the molecular structure of indole is similar to benzofuran and indole is more stable, it is possible to produce indole from furan with active nitrogen source using similar conversion process to CFP.

In this study, we showed that indoles can be produced by thermo-catalytic conversion of biomass-derived furans over zeolites with ammonia as both carrier gas and reactant. To understand the major factors which may influence indole yield and selectivity, in the fixed bed reactor we studied the furan conversion systematically with different catalysts (MCM-41, β -zeolite, ZSM-5 (Si/Al=50) and HZSM-5 with different Si/Al ratios (Si/Al=25, 50, 63, 80), reaction temperature, weight hourly space velocity (WHSV) of furan to catalyst, and the molar ratio of ammonia to furan. Moreover, different bio-derived furans were employed for producing indoles. The stability of the optimal catalyst was also tested. In addition to experiments, we also performed quantum calculations to obtain fundamental insights into the reaction of furan to indole under ammonia atmosphere catalyzed by the acidic zeolite.

Experimental Section

Chemicals

Furan (≥ 99.5 , AR), furfural (≥ 99.5 , AR), ethanol (≥ 99.5 , AR), benzene (≥ 99.5 , AR), toluene (≥ 99.5 , AR), xylene (≥ 99.5 , AR), pyridine (≥ 99.5 , AR), 2-methylpyridine (≥ 99.5 , AR), 3-methylpyridine (≥ 99.5 , AR), 4-methylpyridine (≥ 99.5 , AR) were purchased from Sinopharm Chemical Reagent Co. Ltd. 2-Methylfuran (≥ 99.5 , AR), bi-cyclohexane (≥ 99.5 , AR), benzofuran (≥ 99.5 , AR), pyrrole (≥ 99.5 , AR), aniline (≥ 99.5 , AR), indole (≥ 99.5 , AR), 2-methylindole (≥ 99.5 , AR), 3-methylindole (≥ 99.5 , AR), 4-methylindole (≥ 99.5 , AR), and 2,4-dimethylindole (≥ 99.5 , AR) were purchased from Aladin Chemical Reagent Co. Ltd. All these chemicals were used as received without any further purification. NH_3 (≥ 99.5 , AR), N_2 (99.999%), Ar (99.999%), He (99.999%) and standard gases were purchased from Nanjing Special Gases Factory.

Catalyst and characterization

MCM-41, β -zeolite, ZSM-5 (Si/Al=50) and HZSM-5 with different Si/Al ratios (Si/Al=25, 50, 80) were purchased from the Catalyst Plant of Nankai University. The typical properties of these catalysts are shown in the supplementary information (Table 1). The particle size of the catalysts was about 40 meshes.

The elemental contents of the catalysts were measured by inductively coupled plasma and atomic emission spectroscopy

(ICP/AES, Atomscan Advantage, Thermo Jarrell Ash Corporation, USA). The catalysts were investigated by temperature programmed desorption of ammonia (NH_3 -TPD) and Brunauer–Emmett–Teller surface area (BET) analyses. For the NH_3 -TPD tests, the catalysts were treated at 500 °C under helium flow (ultrahigh purity, 40 mL/min) for 2 h, and the adsorption of ammonia was carried out at 90 °C for 1 h. After that, the catalysts were flushed with helium at 90 °C for 2 h, and the programmed-desorption of NH_3 was run from 90 to 700 °C with a heating rate of 9 °C/min.¹² The desorbed ammonia was measured by a gas chromatograph (GC-SP6890, Shandong Lunan Ruihong Chemical Instrument Co. Ltd., Tengzhou China) with a thermal conductivity detector (TCD). The N_2 adsorption/desorption isotherms of the catalysts were measured at -196 °C using the COULTER SA 3100 analyzer.

Apparatus for thermo-catalytic conversion of furans

As shown in Fig. S1, a bench-top continuous flow reactor consisting of a quartz tube reactor heated by a furnace and a condensation tube bathed in liquid nitrogen was used for these experiments. The catalyst bed supported by quartz wool was built up in the heating zone of the reactor. Furan was fed into the reactor with a peristaltic pump under a certain flow rate and purged with ammonia. Volatile products were trapped in the condensation tube cooled with liquid N_2 .

Computational methods

All calculations were performed with Gaussian 09 program.¹³ Geometry optimizations were conducted in gas phase with the B3LYP function¹⁴ and 6-311G(d,p) basis set. Frequency analysis was performed at the same level of theory to confirm that the optimized structure was either a minimum or a transition state, and also to obtain the thermodynamic corrections at 500 °C. To provide more accurate energies, single point energies of optimized structures were calculated by Truhlar's M06-2X function¹⁵ and a large basis set 6-311++G(2df,2p). The reported energies are the gas-phase single point energies corrected by Gibbs free energy corrections, responding to 1 atm and 500 °C.

Product analysis and data processing

The liquid products were analyzed by GC-MS (Thermo Trace GC Ultra with an ISQ i mass spectrometer) equipped with a TR-35MS capillary column (30 m \times 0.25 mm \times 0.25 mm). Split injection was performed at a split ratio of 50 using helium (99.999%) as carrier gas. The GC heating ramp was: 1) hold at 40 °C for 3 min, 2) heat to 180 °C at 5 °C /min, 3) heat to 280 °C at 10 °C /min, and 4) hold at 280 °C for 5 min.

The total amount of liquid products was determined by the weight difference of the condensation tube before and after the experiment. The coke at the end of the run was measured after the reaction by weighing the solids and subtracting the weight of the catalyst. The carbon yield of coke was further determined by elemental analysis.

The major liquid products were quantitatively determined by gas chromatography (GC 1690, Kexiao, China) employing a 30 m × 0.25 mm × 0.25 μm fused-silica capillary column (HP-Innowax, Agilent). The liquid sample was mixed with bicyclohexane as the internal standard and diluted by ethanol. The GC operating conditions were as follows: carrier gas: nitrogen; injection port: 250 °C in a split mode; detector (FID): 250 °C; column temperature: 40 °C; oven temperature program: heating up to 250 °C at a rate of 10 °C/min, and holding at a final temperature for 5.0 min.

The gas products were collected in gas bags. The gas bags were weighed before and after reaction and their contents were analyzed using gas chromatography (GC-SP6890, Shandong Lu-nan Ruihong Chemical Instrument Co., Ltd., Tengzhou, China) with two detectors, a TCD for analysis of H₂, CO, CH₄, and CO₂ separated on TDX-01 column, and a FID (flame ionization detector) for gas hydrocarbons separated on Porapak Q column. The moles of gas products were determined by the normalization method with standard gas.

The WHSV, the yield of coke, gases, N-containing chemicals, aromatics and the selectivity of different N-containing chemicals, indoles and gases were calculated from Equation 1 to 8.

$$(1) \text{WHSV} = \frac{\text{Mass flow rate of furans}}{\text{Mass usage of catalyst in the catalyst bed}}$$

$$(2) \text{Coke yield (C mol\%)} = \frac{\text{Moles of carbon in solid residue}}{\text{Moles of carbon in feedstocks}} \times 100\%$$

$$(3) \text{Gases yield (C mol\%)} = \frac{\text{Moles of carbon in gases}}{\text{Moles of carbon in feedstocks}} \times 100\%$$

$$(4) \text{N-containing chemicals yield (C mol\%)} = \frac{\text{Moles of carbon in N-containing chemicals}}{\text{Moles of carbon in feedstocks}} \times 100\%$$

$$(5) \text{Aromatics yield (C mol\%)} = \frac{\text{Moles of carbon in aromatics}}{\text{Moles of carbon in feedstocks}} \times 100\%$$

$$(6) \text{N-containing chemicals selectivity (\%)} = \frac{\text{Moles of carbon in specific N-containing chemicals}}{\text{Total moles of carbon in all the N-containing chemicals}} \times 100\%$$

$$(7) \text{Indole selectivity (\%)} = \frac{\text{Moles of carbon in specific indole}}{\text{Total moles of carbon in all indoles}} \times 100\%$$

$$(8) \text{Gas selectivity (\%)} = \frac{\text{Moles of carbon in specific gas}}{\text{Total moles of carbon in gases identified}} \times 100\%$$

Results and discussion

Catalyst property effect on furan conversion with ammonia

Table 1. Typical properties of catalysts used in this study

Catalyst	BET Surface area (m ² /g)	Pore diameter ^a (nm)	Si/Al	Total acid (μmolg ⁻¹)
β-Zeolite	640	0.7	50	683.3
MCM-41	1000	3.8	50	260.0
ZSM-5	420	0.5	50	255.5
HZSM-5-1	350	0.5	50	293.6
HZSM-5-2	370	0.5	25	580.6
HZSM-5-3	370	0.5	63	226.2
HZSM-5-4	375	0.5	80	92.4

a. The data were provided by the manufactures.

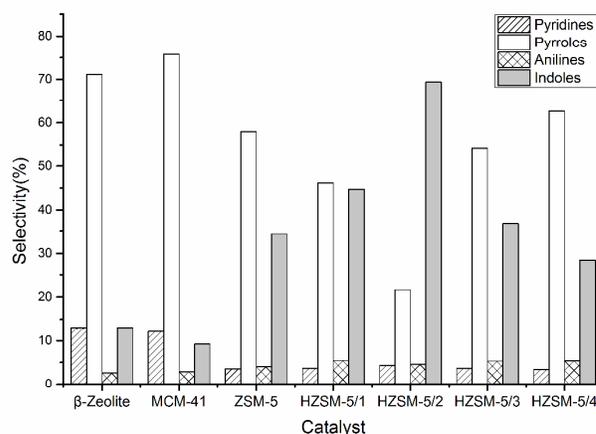


Figure 1. N-containing chemicals selectivity for thermo-catalytic conversion of furan with ammonia over different catalysts.

The appropriate catalyst was essential to selectively obtain target products. Seven catalysts were tested in this study and their typical properties are shown in the supplementary information (Table 1). The detailed furan conversion results over these catalysts at 500 °C are summarized in Table 2. For better comparison, the selectivity of N-containing chemicals are demonstrated in Figure 1. The major classes of products from this reaction were coke, gases, N-containing chemicals and trace amount of aromatics. The N-containing chemicals included pyrroles, indoles, small amount of pyridines and anilines. The detected gases were CO, CH₄, C₂H₄, C₃H₆. Trace amount of CO₂ was also produced during this process. This trace amount of CO₂ was observed from adsorption of product gases in a Ca(OH)₂ solution. However, CO₂ was difficult to be identified by our GC setup because it reacted with ammonia to form ammonium carbonate.

ZSM-5, β-zeolite and MCM-41 tended to catalytically convert furan and ammonia into pyrroles and gases, but not indoles. When furan was catalyzed by β-zeolite and MCM-41, only about 5.6 % and 3.5 % of indoles were produced. The main N-containing chemical was pyrroles, and their selectivity was up to 71% and 75%, respectively. When ZSM-5 was used

Table 2. The detailed product distributions from thermo-catalytic conversion of furan with ammonia over different zeolite catalysts^a.

Entry	1	2	3	4	5	6	7
Catalyst	β -Zeolite	MCM-41	ZSM-5	HZSM-5/1	HZSM-5/2	HZSM-5/3	HZSM-5/4
Si/Al	50	50	50	50	25	63	80
Carbon yield of products (C %)							
Total carbon	96.3	93.9	97.6	94.3	91.5	96.7	97.5
Coke	19.6	12.3	12.1	15.5	21.0	12.9	9.1
Gases	33.6	43.3	25.8	21.5	23.4	10.1	8.8
N-containing chemicals	42.6	38.0	59.0	56.8	45.7	73.0	79.2
Aromatics	0.5	0.3	0.7	0.5	1.4	0.7	0.40
Carbon yield of N-containing chemicals (C %)							
Pyridines	5.6	4.6	2.1	2.1	2.0	2.7	2.7
Pyrroles	30.3	28.8	34.2	26.2	9.9	39.6	49.6
Anilines	1.1	1.1	2.4	3.1	2.1	3.9	4.3
Indoles	5.6	3.5	20.3	25.4	31.7	26.8	22.6
Indole selectivity (%)							
Indole	70.0	80.0	73.6	78.1	74.2	81.4	87.0
2-Methylindole	24.2	15.9	21.4	17.0	21.9	14.1	8.7
3-methylindole	3.1	2.0	2.7	2.3	1.6	1.9	1.7
4-methylindole	0.9	0.6	0.8	0.7	0.8	0.7	0.4
2,4-dimethylindole	0.5	0.3	0.4	0.4	0.1	0.3	0.2
Other alkylindoles ^b	1.3	1.2	1.1	1.0	1.4	1.6	2.0
Gas selectivity ^b (%)							
CO	60.1	73.9	68.2	70.1	73.9	68.2	66.4
CH ₄	5.9	5.6	5.8	5.9	5.6	5.8	7.2
C ₂ H ₄	20.5	14.3	16.0	15.5	14.3	16.0	17.0
C ₃ H ₆	13.5	6.2	9.0	8.5	6.2	9.0	9.4

a. Reaction condition: in all cases, reaction temperature was 500 °C, WHSV was 0.5 h⁻¹, and the ammonia to furan molar ratio was 8:1.

b. 5-methylindole, 6-methylindole, 7-methylindole, 2,3-dimethylindole, 2,5-dimethylindole, etc. b). The CO₂, C₂H₆, C₃H₈ and C₃+olefins (<1%) were neglected in the calculations.

as catalyst, the yield of total N-containing chemicals increased by more than 38% and the distribution changed dramatically. The carbon yield of indoles reached up to 20.3% and the selectivity tripled compared to other catalysts. At the same time, both the yield and selectivity of pyrroles decreased. The results indicated that compared to MCM-41, β -zeolite, the special pore structure of ZSM-5 could promote the formation of indoles.

Changing ZSM-5 to HZSM-5 can introduce acid to the catalyst but keep its pore structure, therefore, HZSM-5/1 with same Si/Al ratio(50) as ZSM-5 was selected to investigate the acid effect. Compared the results in Table 2, entries 3 and 4, the introduction of acid slightly increased the coke but decreased both gases and N-containing chemicals production. However, it increased the indole yield from 20.3% to 25.4% but decreased the pyrrole yield from 34.2 to 26.2%. Since the alumina

contents of the zeolite determine the acid densities and acidities of the catalyst which may influence the product distribution, three other HZSM-5 catalysts with silica to alumina ratios 25, 63 and 80 were also tested. The acid densities of these catalysts determined by NH₃-TPD are shown in Table1, and the NH₃-TPD curves can be seen in the supplementary information Fig. S2. Both the acid density and acidity decreased with the Si/Al ratio increase. As shown in Table 2 entries 4-7, with the Si/Al ratio increased from 25 to 80, the product distribution of this reaction changed a lot. The carbon yield of coke, gases and aromatics decreased from 21.0%, 23.4% and 1.4% to 9.1%, 8.8% and 0.4%, the yield of all the N-containing chemicals increased from 45.7% to 79.2%, respectively. Meanwhile, as shown in Figure1, the product distribution in the N-containing chemicals changed dramatically with the Si/Al ratio of HZSM-

5 increased from 25 to 80. The carbon yield and selectivity of pyrroles increased from 9.9% and 21.7% to 49.6% and 62.6%, while the carbon yield and selectivity of indole decreased from 31.7% and 69.4% to 22.6% and 28.5%. Accordingly, the N-containing product distribution is a strong function of the acid density and acidity. HZSM-5 with Si/Al=25 shows the best activity for thermo-catalytic conversion of furan with ammonia to indoles. It will be used for the following tests.

Temperature effect on furan conversion with ammonia

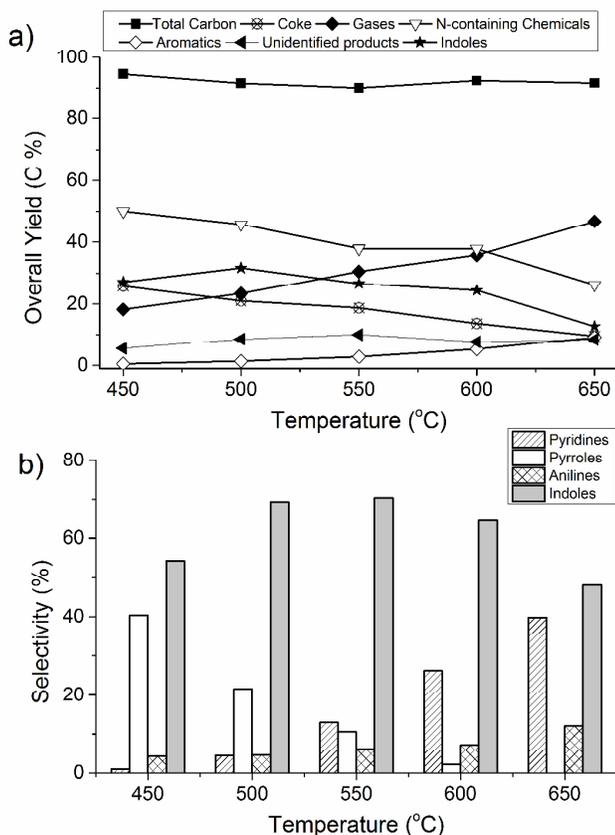


Figure 2. The effect of reaction temperature on thermo-catalytic conversion of furan with ammonia over HZSM-5 (Si/Al=25), (a) overall yield; and (b) N-containing chemicals selectivity.

The temperature effect on this reaction was investigated in the range of 450 °C to 650 °C over HZSM-5 catalyst. WHSV was 0.5 h⁻¹, and the ammonia to furan molar ratio was 8:1. Figure 2 shows the overall carbon yield of coke, gases, N-containing chemicals, aromatic and indoles, (a); the selectivity of product distributions in the N-containing chemicals (b) at different reaction temperatures. The detailed product distribution at different temperatures is given in the supplementary information Table S1. According to Figure 2a, the carbon yield of coke, gases, N-containing chemicals, aromatics and indoles were a strong function of the reaction temperature. With the temperature increasing from 450 to 650 °C, the carbon yield of gases increased from 18.2% to 46.7%, while the carbon yield of coke decreased from 25.8% to 9.5%. It demonstrates that higher temperature promotes furan deep cracking to form non-

condensable gas products. With temperature increasing, N-containing chemicals decreased from 50.0% to 26.3%, while aromatics increased from 0.5% and 9.1%, indicating that aromatics could be one of the downstream products converted from N-containing chemicals. It will be further discussed in the reaction mechanism part.

According to Figure 2b, the distribution of N-containing chemicals also changed dramatically with temperature. The selectivity of pyridines increased and the selectivity of pyrroles decreased with increasing temperature. No pyrroles were detected at 650 °C and the pyridines selectivity was 40% at this temperature. The anilines selectivity in the N-containing chemicals increased from 4.2% to 12.0%. At higher temperature, the cracking reaction became more severe, and many light oxygenated chemicals, such as acetaldehyde *etc.*, could be formed, which could be further converted to pyridines. Thus, the carbon yield and selectivity of pyridines increased a lot with the reaction temperature increasing. The maximum selectivity of indoles in the N-containing chemicals reached 70% at temperatures of 500-550 °C. Combined with the carbon yield of N-containing chemicals shown in the Figure 2a, the maximum yield of indoles could be obtained at about 500 °C.

WHSV effect on furan conversion with ammonia

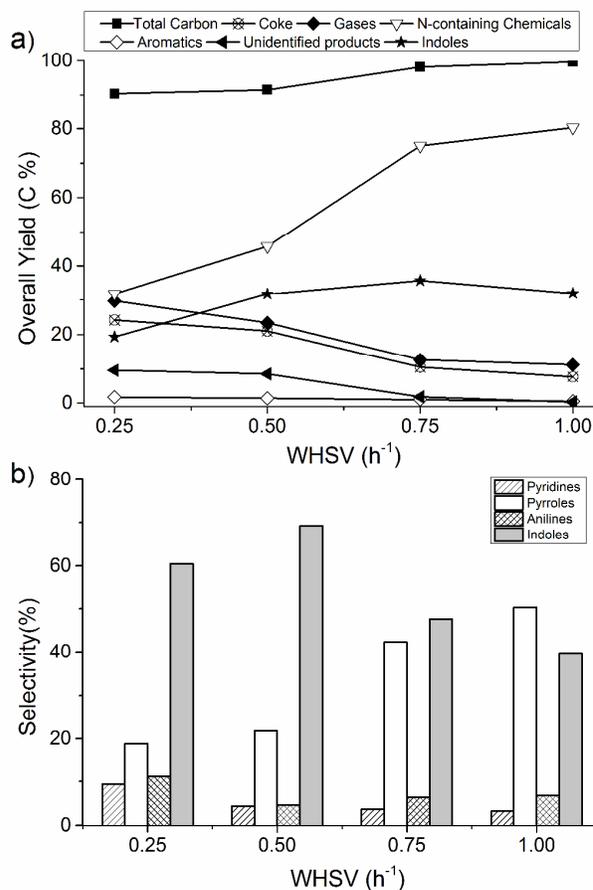


Figure 3. The effect of WHSV on thermo-catalytic conversion of furan with ammonia over HZSM-5 (Si/Al=25), (a) overall yield; and (b) N-containing chemicals selectivity.

The WHSV was defined as the ratio of the mass flow rate of furan to the mass of catalyst used in a reactor. During the experiments, the mass flow rate of furan ranged from 0.5-2 g/h while the mass of catalyst was kept constant at 2 g. The reaction temperature was 500 °C, and the ammonia to furan molar ratio was 8:1. The detailed product distribution of furan conversion with different WHSV is shown in the supplementary information Table S2. Figure 3 demonstrates that the overall yield of coke, gases, N-containing chemicals, aromatics, indoles and the selectivity of N-containing chemicals were a function of WHSV. According to Figure 3a, with the WHSV increased from 0.25 to 1 h⁻¹, the carbon yield of coke and gases decreased from 24.2% and 29.7% to 7.7% and 11.2%, respectively, while the carbon yield of N-containing chemicals increased from 34.8% to 80.3%. It indicated that a lower WHSV could cause the deep conversion of furan over the catalyst to form gas products and coke. Figure 3b shows the selectivity of N-containing chemicals from catalytic conversion of furan with different WHSV. It can be seen that with the WHSV increased from 0.25 to 1 h⁻¹, the selectivity of pyridines and anilines decreased dramatically, while the selectivity of pyrroles increased significantly from 18.9% to 50.3%. Meanwhile, the maximum selectivity of indoles in the N-containing chemicals was obtained at about 0.5 h⁻¹, and the carbon yield and the selectivity reached about 31.7% and 70%, respectively. It indicates that pyridines and anilines could be the down-stream products while pyrroles could be the up-stream products for the furan conversion to indoles and a suitable WHSV for this conversion is very important to maximize the indoles production. A lower WHSV could cause the overreaction of furan over the catalyst to produce more down-stream products, while a higher WHSV would cause the incompletely reaction of furan over the catalyst. As for the desired WHSV for furan to indoles in this study, the maximum carbon yield of indoles, 35.7%, was obtained at 0.75 h⁻¹, while the selectivity of indoles was only about 47.6%. Therefore, the desired WHSV should be in the range of 0.5 to 0.75 h⁻¹.

Ammonia to furan molar ratio effect on furan conversion

The effect of ammonia to furan molar ratio on furan conversion to indoles was investigated at 500°C by fixing the WHSV of furan to catalyst at 0.5 h⁻¹ and the mass usage of catalyst at 2 g, while changing the flow rate of ammonia. Because in this study, the ammonia served not only as the reagent but also as the carrier gas, different flow rate of ammonia would result in different ammonia to furan molar ratio and different reaction time of furan and the intermediate vapors in the system. The results of the effect of ammonia to furan molar ratio are shown in Figure 4. The detailed product distributions of furan conversion with different ammonia to furan molar ratios are given in the supplementary information Table S3. As shown in Figure 4a, with the ammonia to furan molar ratio increasing, the overall yield of coke and gases decreased, while the overall yield of N-containing chemicals increased. The yield of

aromatics kept constant. It demonstrates that ammonia promotes the furan conversion to N-containing chemicals.

Figure 4b shows that as the molar ratio increased, the selectivity of pyrroles increased significantly from 10.0% to 49%, while the selectivity of indoles, pyridines and anilines decreased, and the selectivity of indoles in the N-containing chemicals decreased from 75% to 45%. During this process, a higher ammonia to furan molar ratio, that is, a higher ammonia flow rate could cause the catalytic reaction time of reactant and intermediate vapors over the catalysts decreased, and would cause the reaction from furan to indoles not sufficient. Thus, as the ammonia to furan molar ratio increased, the selectivity of indoles, pyridines and anilines decreased, while the selectivity of pyrroles increased. These results are also in agree with those from temperature and WHSV tests that pyridines and anilines could be the down-stream products while pyrroles could be the up-steam products for the furan conversion to indoles. When the ammonia to furan ratio was at the range of 2 to 8, the carbon yield of indoles didn't change much, which was kept around 32%. Therefore, 2 should be chosen as the suitable molar ratio of ammonia to furan to produce indoles.

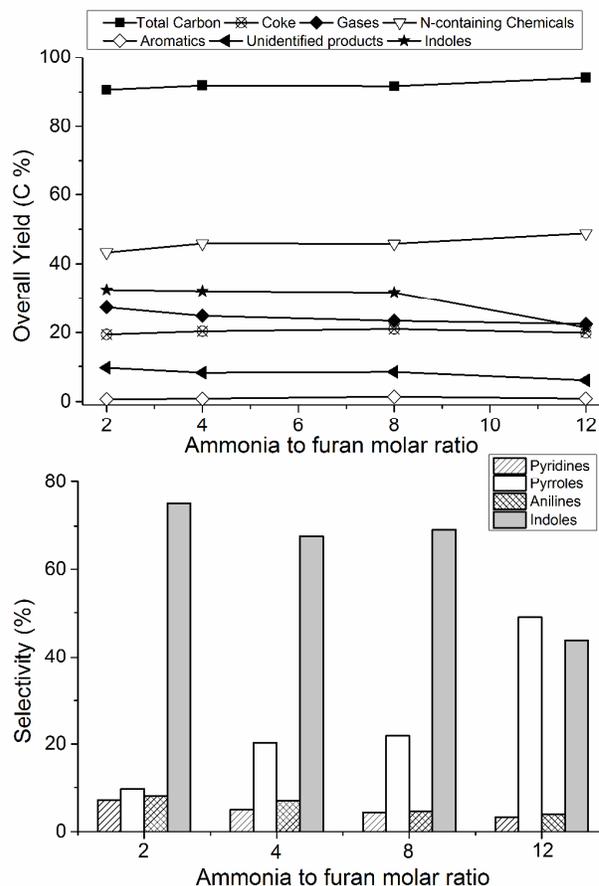


Figure 4. The effect of molar ratio on thermo-catalytic conversion of furan with ammonia over HZSM-5 (Si/Al=25), (a) overall yield; and (b) N-containing chemicals selectivity.

Table 3. The detailed product distributions converted from different bio-derived furans with ammonia. ^a

Entry	1	2	3	4
Feedstocks	MF	MF	FR+MF ^b	FR+MF ^b
Tem. (°C)	500	600	500	600
The carbon yield of products (C %)				
Total carbon	90.4	91.2	91.7	91.8
Coke	22.0	14.2	22.8	18.7
Gases	28.2	39.6	27.4	33.6
N-containing chemicals	38.1	32.2	40.1	36.7
Aromatics	1.7	5.2	1.4	2.9
Overall carbon yield of N-containing chemicals (C %)				
Pyridines	2.3	10.0	2.4	6.8
Pyrroles	10.6	2.7	10.3	5.4
Anilines	0.9	1.9	1.0	1.7
Indoles	24.3	17.6	26.4	22.8
The selectivity of indoles (%)				
Indole	15.7	52.0	32.5	58.7
2-Methylindole	32.3	26.4	38.1	9.3
3-methylindole	8.0	5.6	4.2	3.2
4-methylindole	6.8	2.8	4.3	6.6
2,4-dimethylindole	33.4	3.8	17.0	13.9
Other alkylindoles ^c	3.8	9.4	3.9	8.3

a. Reaction condition: In all cases, WHSV was 0.5 h⁻¹ and the ammonia to furan molar ratio was 8:1. b. The mole ratio of furan to 2-methylfuran was 1:1; c. 5-methylindole, 6-methylindole, 7-methylindole, 2,3-dimethylindole, 2,5-dimethylindole, etc.

Thermo-catalytic conversion of different bio-derived furans with ammonia to indoles

In this study, the production of indoles from bio-derived 2-methylfuran (MF) and the mixture of furan and 2-methylfuran (FR+MF) with ammonia were also investigated. Table 3 shows the carbon yield of coke, gases, aromatics, N-containing chemicals and the carbon selectivity of indoles from the different furans to indoles. It can be seen that indoles are still the main products in the N-containing chemicals. With temperature increasing from 500 °C to 600 °C, the carbon yield of indoles and pyrroles decreased, while the carbon yield of aromatics, pyridines and anilines increased. Meanwhile, the distribution of indole compounds changed significantly. As shown in Table 3, whether MF or the mixture of MF and FR served as feedstock, when the reaction temperature was at 500 °C, the main compounds were alkyl indoles, especially, 2-methylindole and 2,4-dimethylindole; However, when the reaction temperature was at 600 °C, the main compound changed to indole, and alkyl indoles became the side products. used as the feedstock. Moreover, when furan reacted with ammonia, no benzofuran was detected. Therefore, benzofuran should not be an intermediate in indole formation.

According to Table 4, when pyrrole was employed as the feedstock and undergoes the thermo-catalytic conversion process with ammonia, the product distribution was much

As the reaction temperature increased, MF prone to undergo a cracking reaction to form furan, which could be the reason that the selectivity of indole increased a lot from 500 °C to 600 °C.

It is worth noting that when furan was the feedstock, the main compound was indole with a carbon selectivity of 75%. However, when MF was the feedstock under the same reaction conditions, the main compounds were 2-methylindole and 2,4-dimethylindole, with carbon selectivity of 32.3% and 33.4%, respectively. When the feedstock was changed to the mixture of MF and FR, the main compounds were 2-methylindole and indole, and the carbon selectivity of them was 38.1% and 32.5%, respectively. It indicated that via the coupling reaction, different type of indoles can be selectively produced by using different furanic compounds as feedstock with ammonia under proper conditions.

Mechanism from furan to indole

Because to our best knowledge, there is no report previous on the mechanism by which indole is made from furanic compounds with ammonia, in this study, we performed experiments and quantum calculations to obtain fundamental insights into this reaction.

Previous studies showed that furan can be converted to benzofuran and then form aromatics.^{10a,10d,11} Under ammonia atmosphere, furan might form benzofuran and then benzofuran reacts with ammonia to form indole. However, when benzofuran reacted with ammonia under selected conditions, the conversion of benzofuran was only 24.2%. The main products were aromatics, aniline and indoles, and the selectivity ratio of aromatics to indoles in the products was about 1:1 (Table 4). It means if furan went through benzofuran pathway to indoles, aromatics should be one of the major products, but only trace amount of aromatics were detected when furan was

Table 4. Summary of thermo-catalytic conversion of different feedstocks with ammonia for mechanism study.

Feedstock	Furan	Benzofuran	Pyrrole	Indole
Conversion (%)	100	24.2	82.4	15.8
Total Carbon (%)	91.5	22.5	79.9	14.9
Coke	21.0	6.1	22.3	4.7
Gases	23.4	2.7	14.6	2.5
N-containing chemicals	45.7	8.9	40.4	6.6
Aromatics	1.4	4.8	2.6	1.1
Overall carbon yield of N-containing chemicals (%)				
Pyridines	2.0	0.3	8.4	2.8
Pyrroles	9.9	N.D	-	N.D
Anilines	2.1	3.6	3.5	3.8
Indoles	31.7	5.0	28.8	-

Reaction conditions: Temperature was 500 °C; the Si/Al of HZSM-5 was 25; WHSV was 0.5 hr⁻¹; the molar ratio of ammonia to furan was 8:1.

closed to the one using furan as the feedstock under same reaction conditions. All these results suggest that pyrrole is the key intermediate from furan to indole.

Whether indole is formed from furan and pyrrole or only from pyrroles requires further investigation. Firstly, we checked the pathway of the transformation of pyrrole and furan into indole. Here, ring-opening and Diels-Alder mechanisms were considered with the aid of density functional theory (DFT) calculations.

As shown in Figure 5, ring-opening mechanism starts from the ring-opening of furan to generate the intermediate CP1. Then CP1 alkylates the pyrrole at the more electronic-rich C2 position to afford CP2 (Figure S3).¹¹ Thereafter, ring-closing occurs via transition state TS1 by the C–C bond formation at the C3 site of pyrrole. The intermediate CP3 is generated after

TS1 and followed by a rapid deprotonation via TS2. Finally, the dehydration of the resulting intermediate CP4 affords the product indole and finishes the catalytic cycle. Ring closing is the rate-determining step in ring-opening mechanism due to the disruption of aromaticity of pyrrole ring and the decrease of entropy in this step. On the other hand, Diels-Alder mechanism starts from the [2+2] addition of pyrrole and furan via transition state TS3. CP5 is formed after TS3 and the following acid-induced ring-opening and dehydration afford indole as the product. However, because the aromaticities of pyrrole and furan are both disrupted in TS3, making TS3 much energetically higher than TS1, therefore ring-opening mechanism is favored over Diels-Alder mechanism. Note that a similar result was also obtained with the theoretical studies by Auerbach et al. on the transformation of furan to benzofuran.

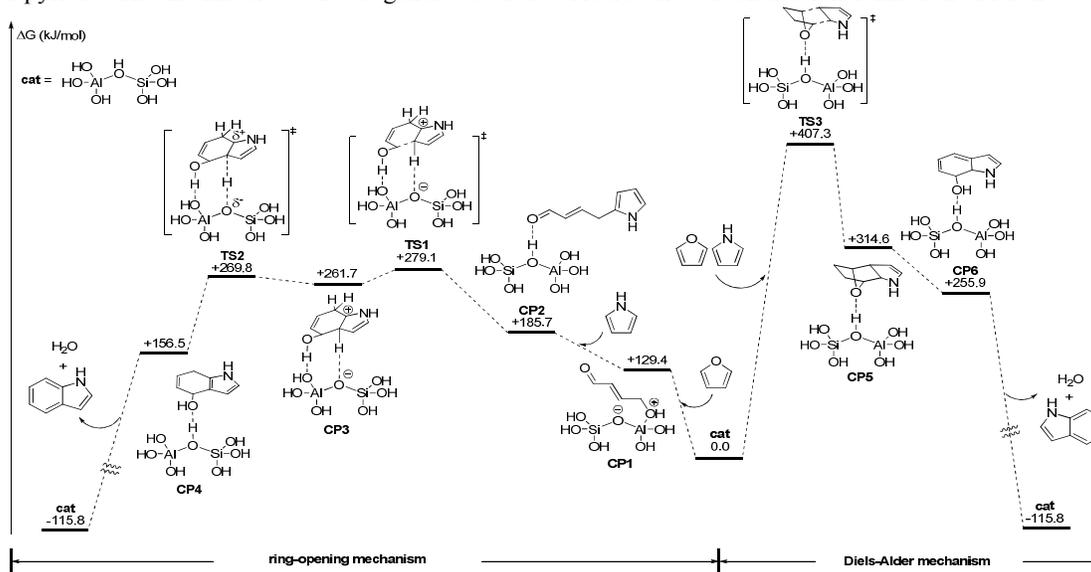


Figure 5. Energy profile of ring-opening and Diels-Alder Mechanisms.

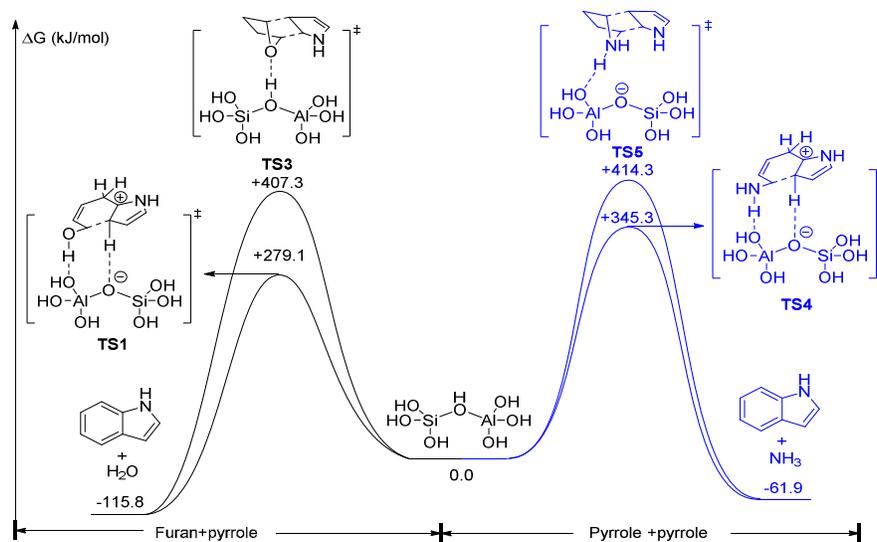


Figure 6. Comparison of ring-opening and Diels-Alder mechanisms for different substrates.

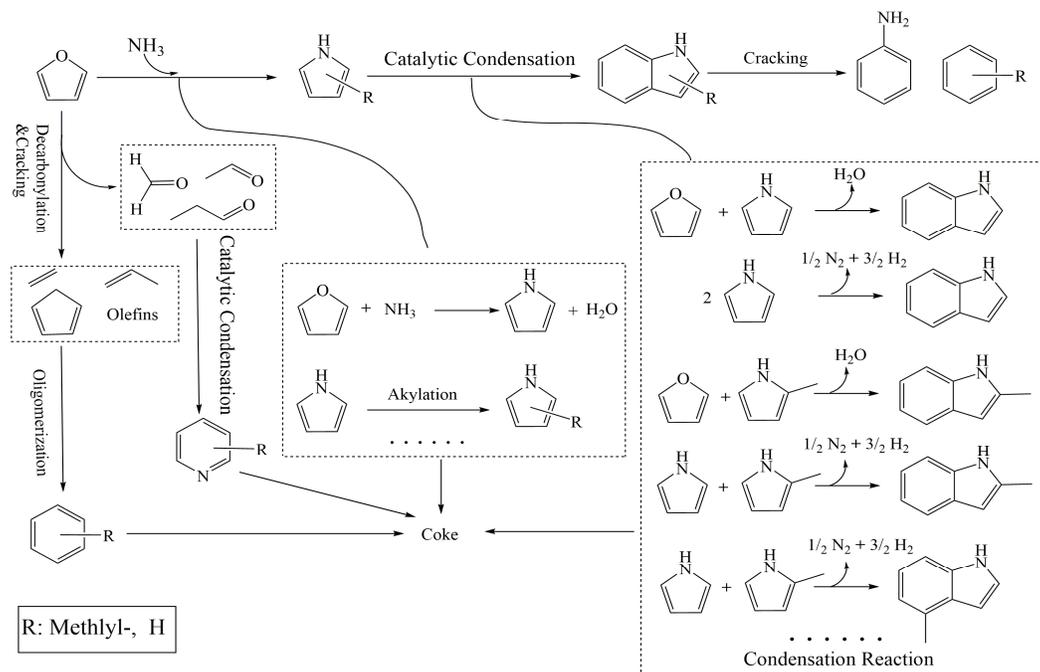


Figure 7. The proposed reaction pathways for the production of indoles from furan via catalytic thermochemical conversion process with ammonia over HZSM-5.

We also compared the two mechanisms with only pyrrole as the substrates (Figure 6), and ring-opening mechanism is found to be favored over Diels-Alder mechanism on this condition (TS4 vs TS5). Besides, the free energy of TS4 is higher than that of TS1 by about 66 kJ/mol. Based on the overall calculations, from furan to indole, ring-opening is the more favorable mechanism, and the pyrrole + furan is the more favorable pathway.

Besides indoles, small amount of aniline was also produced from furan and pyrrole. Considering the molecules structure, aniline should not form directly from either furan or pyrrole. When indole was used as the feedstock, aniline was the only detected N-containing compound in the organic liquid products. Meanwhile, certain amount of aromatics (mainly benzene) was produced. Our tests confirmed that benzene could not react with ammonia to form any N-containing compounds under selected conditions. Therefore, aniline is produced from indole.

Based on all above investigation, the reaction pathways for the production of indoles by thermo-catalytic conversion bio-derived furans with ammonia is proposed and summarized in Figure 7. Furan initially reacted with ammonia to form pyrrole and some alkyl pyrroles (eg: 2-methylpyrrole, etc). The alkyl pyrroles were formed from pyrrole which underwent the alkylation with the alkanes produced from the cracked furans and other molecules. The detailed mechanism has been reported by previous study.¹⁶ Then the pyrrole reacted with furan or pyrrole to form indole via the ring-opening or Diels-Alder condensation way. At the same time, alkyl pyrroles reacted with pyrrole, furan or alkyl pyrroles to form alkyl indoles. Indoles can further decomposed to aniline and aromatics. Meanwhile, furan may undergo the cracking and decarbonylation reaction to form olefins and oxygenated

chemicals, which could be further converted to aromatics and pyridines. Meanwhile, small amount of pyridines could also be formed from the cracking intermediates of pyrroles. Coke, CO_x, hydrocarbons and H₂O were also produced during the whole process as the side products.

Conclusions

This study demonstrated that indoles can be synthesized directly from bio-derived furans in the fixed bed reactor with ammonia over acidic catalysts at elevated temperature. Ammonia served not only as the carrier gas, but also as the reactive nitrogen source. Among different catalysts, HZSM-5 with Si/Al ratio as 25 showed best reactivity for indoles production due to the desired pore structure and acidity. Temperature displayed significant effect on the product distribution. The maximum yield of indoles was obtained at moderate temperature around 500°C. The WHSV of furan to catalyst investigation indicated that a lower WHSV could cause the overreaction of furan over the catalyst to produce more aniline and pyridines, while a higher WHSV would cause the incomplete reaction of furan. The desired WHSV was in the range of 0.5 to 0.75 h⁻¹. Because ammonia served as both reactant and carrier gas, to supply sufficient reactant and keep desired reaction time, appropriate ammonia to furan molar ratio was important on furan conversion to indoles. Under the optimal conditions, the highest total carbon yield and indoles selectivity in the N-containing chemicals was 32% and 75%, respectively. The primary coupling reaction of different bio-derived furans can produce alkyl indole products, such as 2-methylindole and 2,4-dimethylindole. Based on the overall calculations and experiments, from furan to indole, ring-

opening is the more favorable mechanism compared to the Diels-alder mechanism, and the pyrrole + furan pathway is more favorable compared to the pyrrole + pyrrole pathway.

It is worth to mention that based on our study, indoles can be produced from furanic compounds, which are the important intermediates in the biomass pyrolysis process. Therefore indoles could also be produced by thermo-catalytic conversion of real biomass with ammonia at the proper conditions, which would make it possible to extend the starting material for producing indoles to abundant biomass.

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Notes and references

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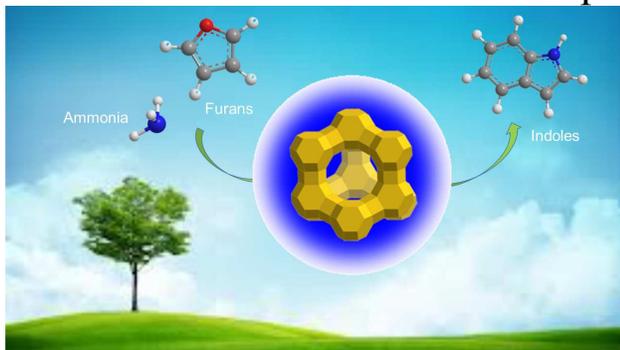
† Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

Electronic Supplementary Information (ESI) available: [The scheme of the apparatus, the NH₃-TPD spectra of the catalysts, The geometry-optimized structures and ground state electronic energies of the three protonated pyrrole, and the detailed product distribution from thermo-catalytic conversion of furan with ammonia at different reaction conditions]. See DOI: 10.1039/b000000x/

- 1 a) R. J. Sundberg, *Indoles*, Academic Press, San Diego, 1996; b) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev.*, 2010, **110**, 4489 c) K. Krüger née Alex, A. Tillack, M. Beller, *Adv. Synth. Catal.*, 2008, **350**, 2153; d) T. Kawasaki, K. Higuchi, *Nat. Prod. Rep.*, 2005, **22**, 761; e) Wang C, Sun H, Fang Y, *Angew. Chem., Int. Ed.*, 2013, **125**, 5907.
- 2 a) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.*, 2006, **106**, 2875; b) S. Cacchi, G. Fabrizi, *Chem. Rev.*, 2005, **105**, 2873; c) S. Cacchi, G. Fabrizi, *Chem. Rev.*, 2011, **111**, 215; d) M. M. Inman, C. J. Moody, *Chem. Sci.*, 2013, **4**, 29, e) c; f) R. Bernini, S. Cacchi, G. Fabrizi, G. Forte, F. Petrucci, A. Prastaro, S. Niembro, A. Shafir, A. Vallribera, *Green Chem.*, 2010, **12**, 150; g) M. Platon, R. Amardeil, L. Djakovitch, J. C. Hierso, *Chem. Soc. Rev.*, 2012, **41**, 3929.
- 3 a) E. Fischer and F. Jourdan, *Ber. Dtsch. Chem. Ges.*, 1883, **16**, 2241; b) Robinson, *The Fischer Indole Synthesis*, John Wiley & Sons Inc., New York, 1982.
- 4 A. Bischler and H. Brion, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 2860; b) A. Bischler and P. Firemann, *Ber. Dtsch. Chem. Ges.*, 1893, **26**, 1336.
- 5 C. Graebe, F. Ullmann, *Ann.*, 1896, **291**, 16.
- 6 a) C. D. Nenitzescu, *Bull. Soc. Chim. Romania*, 1929, **11**, 37; b) M. Bosco, R. Dalpozzo, G. Bartoli, G. Palmieri and M. Petriani, *J. Chem. Soc., Perkin Trans.*, 2, 1991, 651; c) P. G. Gassman, T. J. van Bergen and G. Gruetzmacher, *J. Am. Chem. Soc.*, 1973, **95**, 6508; d) a) G. W. Huber, S. Iborra and A. Corma, *Chem. Rev.*, 2006, **106**, 4044; b) A. V. Bridgwater, *Int. J. Global Energy Issues*, 2007, **27**, 160; c) G. W. Huber, J. N. Chheda, C. J. Barrett and J. A. Dumesic, *Science*, 2005, **308**, 1446; d) R. C. Saxena, D. K. Adhikari and H. B. Goyal, *Renewable Sustainable Energy Rev.*, 2009, **13**, 156; e) R. D. Cortright, R. R. Davda and J. A. Dumesic, *Nature*, 2002, **418**, 964; f) E. L. Kunkes, D. A. Simonetti, R. M. West, J. C. Serrano-Ruiz, C. A. Gartner and J. A. Dumesic, *Science*, 2008, **322**, 417.
- 8 a) R. J. van Putten, J. N. M. Soetedjo, E. A. Pidko, J. C. van der Waal, E. J. M. Hensen, E. De Jong and H. J. Heeres, *ChemSusChem*, 2013, **6**, 1681; b) B. Saha and M. M. Abu-Omar, *Green Chem.*, 2014, **16**, 24.
- 9 a) Y. Zhao, T. Pan, Y. Zuo, Q.-X. Guo and Y. Fu, *Bioresour. Technol.*, 2013, **147**, 37; b) W.-L. Fanchiang and Y.-C. Lin, *Appl. Catal., A*, 2012, **419–420**, 102; c) T. R. Carlson, Y. T. Cheng, J. Jae and G. W. Huber, *Energy Environ. Sci.*, 2011, **4**, 145; d) T. R. Carlson, G. A. Tompsett, W. C. Conner and G. W. Huber, *Top. Catal.*, 2009, **52**, 241; e) T. R. Carlson, T. R. Vispute and G. W. Huber, *ChemSusChem*, 2008, **1**, 397; f) H. Y. Zhang, Y. T. Cheng, T. P. Vispute, R. Xiao and G. W. Huber, *Energy Environ. Sci.*, 2011, **4**, 2297; g) A. Zheng, Z. Zhao, S. Chang, Z. Huang, K. Zhao, H. Wu, X. Wang, F. He and H. Li, *Green Chem.*, 2014, **16**, 2580; h) S. Tan, Z. Zhang, J. Sun, & Q. Wang, *Chin. J. Catal.*, 2013, **34**, 641-650; i) C. Liu, H. Wang, A. M. Karim, J. Sun, Y. Wang, *Chem. Soc. Rev.*, 2014, DOI: 10.1039/C3CS60414D.
- 10 a) Y. T. Cheng, Z. P. Wang, C. J. Gilbert, W. Fan and G. W. Huber, *Angew. Chem., Int. Ed.*, 2012, **51**, 11097; b) Y. T. Cheng and G. W. Huber, *Green Chem.*, 2012, **14**, 3114; c) Y. T. Cheng, J. Jae, J. Shi, W. Fan, & G. W. Huber, *Angew. Chem., Int. Ed.*, 2012, **124**, 1416; d) Y. T. Cheng, & G. W. Huber, *ACS Catal.*, 2011, **1**, 611.
- 11 S. Vaitheeswaran, S. K. Green, P. Dauenhauer, S. M. Auerbach, *ACS Catal.*, 2013, **3**, 2012.
- 12 P. Y. Bi, Y. N. Yuan, M. H. Fan, P. W. Jiang, Q. Zhai, Q. X. Li, *Bioresour. Technol.*, 2013, **136**, 222.
- 13 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Jr. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Revision D.01*, Wallingford CT, 2013.

- 14 a) Becke, A. D. *J. Chem. Phys.*, 1993, **98**, 5648. b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B*, 1988, **37**, 785.
- 15 Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215.
- 16 E. Baltazzi, & L. I. Krimer, *Chem. Rev.*, 1963, **63**, 511.

Graphic abstract



Direct production of indoles via thermo-catalytic conversion of bio-derived furans with ammonia over zeolites

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