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Rational design of efficient steric catalyst for isomerization of 2-methyl-3-butenenitrile

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ARTICLE INFO	ABSTRACT
Keywords: Isomerization 2-Pentenenitrile 2-Methyl-2-butenenitrile Density functional theory calculatoins Steric effect	The catalytic isomerization of 2-methyl-3-butenenitrile (2M3BN), a model reaction in the DuPont process, has been performed using NiL ₄ (L=tri- <i>O</i> - <i>p</i> -tolyl phosphite) as a catalyst. The lowered catalytic activity in the isomerization with coexistence of 2-pentenenitrile (2PN) and 2-methyl-2-butenenitrile (2M2BN) indicates that both 2PN and 2M2BN are the catalyst inhibitors, and the quantitative relationship between the conversion of 2M3BN and the content of 2M2BN and 2PN is provided. DFT calculation results suggest that the inhibition effect is attributed to the generation of dead-end intermediates (2PN)NiL ₂ and (2M2BN)NiL ₂ , both of which take nickel atom out of the catalytic cycle in the isomerization process. To suppress the inhibition effect, new catalytic intermediates are rationally designed based on their computational $%V_{bur}$. An efficient method that adding extra ligand 1, 5-bis(diphenylphosphino)pentane (dppp5) to the NiL ₄ catalyst is selected experimentally. Compared to the results obtained with NiL ₄ as catalyst, the (dppp5)NiL ₂ increases the conversion of 2M3BN from 74.5 % to 93.4 % at 3 h of reaction and provides a high selectivity to 3PN (> 98 %) at optimal conditions.

1. Introduction

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The synthesis of adiponitrile (AdN) from 1, 3-butadiene and hydrogen cyanide (HCN) catalyzed by Ni(0)-phosphite complex, which is known as the DuPont process, has received extensive attention [1-3]. In general, the DuPont process includes three steps : the initial hydrocyanation of 1, 3-butadiene to form a mixture of 2-methyl-3-butenenitrile (2M3BN) and 3-pentenenitrile (3PN), the isomerization of 2M3BN to 3PN, and the subsequent C=C double bond migration and a second hydrocyanation to product AdN. Among these steps, the isomerization of 2M3BN to 3PN via a C-CN bond breaking and forming reaction is a key step because it governs the economic profit of the DuPont process. In addition, there is a close relationship between the hydrocyanation and isomerization reactions on the typical catalysts such as NiL₄ (L = tri-O-p-tolyl phosphite) [4]. To facilitate the development of the catalyst used in the DuPont process, the isomerization has been widely used as a model reaction for catalyst evaluation [5-8] and mechanistic investigation [9–12].

Due to its importance of the isomerization reaction for the DuPont process, it has been extensively studied [1,3]. The ligand effects [13] are well-understood thanks to the systematic and meticulous work of Tolman et al., such as the electronic factor [14] and steric factor [15]. These two factors are powerful approaches for explanation of the influence of phosphorus (III) ligands on the catalytic performance, and they are also considered as the basis for rational design of better catalysts. Typically, the catalyst performance depends on the ligand used, and extensive work has been done to optimize the ligands for the isomerization reaction [1,3]. Lewis acids such as $ZnCl_2$ are found to accelerate this reaction [16]. Solvents have a significant effect on the selectivity to 3PN, and nonpolar solvents favor C-CN cleavage in 2M3BN [17]. The key development in the isomerization is to investigate the bidentate ligands, such as diphosphines and diphosphites [6,7,9,10,18,19]. These bidentate ligands can significantly enhance the catalytic activity. Moreover, based on the crystal structure of Ni(η^3 -1-Me-C₃H₄)(CN)(dppb), a reaction mechanism of the isomerization has been proposed [9], which involves five steps : (i) coordination of 2M3BN with nickel via its C=C

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Abbreviations: 2M3BN, 2-methyl-3-butenenitrile; 3PN, 3-pentenenitrile; 2PN, 2-pentenenitrile; 2M2BN, 2-methyl-2-butenenitrile; 4PN, 4-pentenenitrile; AdN, adiponitrile; HCN, hydrogen cyanide; COD, 1, 5-cyclooctadiene; L, tri-*O*-*p*-tolyl phosphite; mL, tri-*O*-*m*-tolyl phosphite; oL, tri-*O*-*o*-tolyl phosphite; dppe, 1,2-bis (diphenylphosphino)ethane; dppp3, 1,3-bis(diphenylphosphino)propane; dppb, 1, 4-bis(diphenylphosphino)butane; dppp5, 1, 5-bis(diphenylphosphino)pentane; dpph, 1,6-bis(diphenylphosphino)hexane; dppf, 1,1'-bis(diphenyphosphino)ferrocene; Xantphos, 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene; XantN, 4,6-Bis (diphenylphosphino)phenoxazine.

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bond, (ii) C—CN bond breaking and formation of a σ -allyl species, (iii) isomerization to the π -allyl species, (iv) σ -allyl formation, and (v) C—CN bond coupling to 3PN coordination. More recently, some mechanistic details [8,11,12], including oxidative addition of 2M3BN, conformational rearrangement and reduction elimination forming 3PN, have been discussed based on DFT calculations [20,21].

In the DuPont process, the conversion of 2M3BN to 2-methyl-2-butenenitrile (2M2BN) and that of 3PN to 2-pentenenitrile (2PN) inevitably occur as side reactions, as shown in Scheme 1, because the conjugated 2M2BN and 2PN are more stable thermodynamically. Therefore, 2M2BN and 2PN always exist in the DuPont process. These by-products reduce the 3PN yield and they cannot be converted to AdN by subsequent hydrocyanation. Using dppb [8,9] or dppf [6] as ligand can provide a high selectivity to 3PN (>98 %). However, expensive organic nickel complex such as Ni(COD)₂ (COD : 1, 5-cyclooctadiene) must be used as the nickel source, which limits their industrial applications. Therefore, it is desired to improve the catalytic selectivity to 3PN in a cheaper way. Despite of the importance of this topic, there are limited researches concerning the formation of 2M2BN and 2PN. In general, commercially available 2M3BN contains \sim 30 % other nitriles (see Supplementary material). It is unclear how the presence of 2M2BN and 2PN changes the catalytic activity and selectivity. In addition, it is difficult to remove 2M2BN and 2PN from 2M3BN by traditional distillation because they have very close boiling points (2M2BN: 115~120°C, 2M3BN: 124°C, 2PN: 127°C). Hence, it is urgently required to figure out the negative effects of undesired 2M2BN and 2PN and develop an efficient strategy to increase the selectivity to 3PN in the isomerization of 2M3BN.

In this work, the isomerization of 2M3BN to 3PN using NiL₄ as the catalyst was studied as the model reaction. It was found that 2M2BN and 2PN had a significant inhibition effect on the activity of the NiL₄ catalyst. DFT calculations were carried out to understand this inhibition effect. A catalytic mechanism was proposed, in which the inhibition by 2M2BN and 2PN was attributed to the formation of (2M2BN)NiL2 and (2PN)NiL2 that made the NiL4 catalyst off-cycle of the reaction. Based on the structural differences of phosphorus ligands, suitable ligands were used to modify the NiL₄ catalyst to increase its selectivity to 3PN. Due to the steric effect, the modification of the NiL₄ catalyst by dppp5 effectively suppressed the inhibition effect of 2M2BN and 2PN in the 2M3BN isomerization reaction, increasing the 2M3BN conversion from 75.4 % to 93.5 % and the 3PN selectivity from 90 % to 98 %.

2. Materials and methods

2.1. Experimental methods

All the catalyst (NiL₄) synthesis experiments were performed with standard Schlenk techniques and all the isomerization reactions were performed in glove box techniques under dry nitrogen with the concentration of oxygen and water below 0.1 ppm, and the entire operation process does not involve water and oxygen. Nitiriles (2M3BN, 3PN, 2PN, and 2M2BN) were purchased from J&K, ligands were purchased from Laajoo, and the other chemicals (Ni(NO₃)₂, ZnCl₂, cumene, toluene, and



octane) were purchased from Aladdin. These nitriles were used as received without purification. Gas chromatograph (GC, Purui Instrument Company, Beijing) was used to analyze the product mixture and the ReactIR¹⁵ technology (METTLER TOLEDO) was employed to monitor the kinetic information of the isomerization process. ³¹P NMR spectra were recorded using BRUKER 600 MHz nuclear magnetic resonance spectrometer with cumene as solvent. And X-ray data was collected on a Rigaku SuperNova AtlasS2 diffractometer equipped with an Atlas CCD detector (see Supplementary material).

The isomerization reactions were performed in a glove box as follows (also called common conditions): 1 mmol NiL₄ catalyst, 5 mmol ZnCl₂, 1 mmol ligand, and 10 mL cumene were added to a three-necked flask and were thoroughly mixed. The reaction system was kept at 100 °C for 30 min, then 2M3BN (72.8 % 2M3BN or 90 % 2M3BN, see Supplementary material) was added to the above system. Samplings (0.1 mL) were taken out every hour, which were centrifuged and analyzed using GC. To test the effect of 2M2BN and 2PN on the activity of the NiL₄ catalyst, a certain amount of 2M2BN or 2PN was added to 90 % 2M3BN to obtain 2M3BN with different contents of 2M2BN or 2PN. Herein, to get the mixed nitriles containing 20 % 2M2BN, 0.65 mL 2M2BN is added to 3.23 mL 90 % 2M3BN. Similarly, 0.80 mL 2PN is added to 3.26 mL 90 % 2M3BN to provide the mixed nitriles containing 20 % 2PN. (see Supplementary material)

2.2. Computational methods

All calculations were carried out using the Gaussian 09 program [22]. The geometry optimizations and calculations of the zero-point vibrational energies (ZPVEs) were performed in the gas phase using the B3LYP [23,24] functional with the SDD [25] basis set for Ni and 6-31 G(d) [26] basis set for C, H, N, O and P. The optimized structures were verified by the calculated vibrational frequencies. No imaginary frequencies were found for the optimized structures that correspond to local minima on the potential energy surface. On the basis of the gas-phase optimized geometries, the solvation effect was incorporated with the SMD solvent model [27]. The solution-phase Gibbs free energy was calculated by adding the correction of the Gibbs free energy in the gas phase to the electronic energy in the solvent. All energies discussed in this work were Gibbs free energies. The buried volume values V_{bur} of the nitriles and intermediates were calculated using SambVca 2.0 [28, 29]. The crystal structures were drawn by the Ortep3 program [30], and the CYLview [31] was employed to represent the intermediates.

3. Results and discussion

3.1. Inhibition effect of 2M2BN and 2PN

To clarify the effect of 2M2BN and 2PN on the activity of the NiL₄ catalyst, the isomerization of 2M3BN was used as the model reaction. The 2M3BN of 90 % purity is known as the purest, although it contains 7% 2M2BN and 3% 2PN. For each experiment, after the isomerization reaction proceeded for 4 h, the nitriles were carefully distilled from the mixture under reduced pressure (10 kPa) and 60 °C, then a second aliquot of 2M3BN was added to the system. As shown in Fig. 1, the conversion of 2M3BN was 74.0 % at 1 h when using 90.0 % 2M3BN as reactant (Fig. 1(a)), while it decreased to 35.5 % when 72.8 % 2M3BN was used (Fig. 1(b)), and it took 3 h that the conversion reached to 74.5 %. The concentrations of 2M2BN and 2PN were only the factor that varied, while other factors remained unchanged. These results showed that 2M2BN and 2PN had an inhibition effect on the NiL_4 catalyst in the 2M3BN isomerization reaction. In addition, the catalytic activity further dropped as the aliquot of 2M3BN ((a): 90 % 2M3BN, (b): 72.8 %2M3BN) was added to the reaction system.

Next, a varied amount of 2M2BN or 2PN was added to the 90 %2M3BN to further study which one or both have the effect on the catalytic activity of the NiL₄ catalyst. As shown in Fig. 1(c), the reaction rate

K. Liu et al.



Fig. 1. The catalytic results of NiL₄ using different 2M3BN as reactants. ^[a] (a) 90.0 % 2M3BN, (b) 72.8 % 2M3BN, (c) 2M2BN and (d) 2PN were added to the 90 % 2M3BN, and (e) and (f) dppp5 was added to reaction system.

^[a] For (a), (b), (c) and (d), NiL₄: L: ZnCl₂: 2M3BN = 1:1:5:30, *T* = 100 °C, and 10 mL cumene; for (e), NiL₄: dppp5: 2M3BN = 1:1:30, *T* = 100 °C, and 10 mL cumene; for (f), NiL₄: dppp5: 2M3BN = 1:1:30, *T* = 100 °C, and 10 mL cumene; for (f), NiL₄: dppp5: 2M3BN = 1:1:30, *T* = 110 °C, and 10 mL cumene.

decreased significantly as the amount of 2M2BN was increased from 7% to 50 %. A rapid decrease in catalytic activity was also observed with the addition of 2PN (Fig. 1(d)). Apparently, both 2M2BN and 2PN are catalytic inhibitors. The formations of 2M2BN and 2PN not only decreased the yield of 3PN, but also decreased the activity of the NiL₄ catalyst in the isomerization of 2M3BN. Moreover, 2PN showed a stronger inhibition effect than 2M2BN, as revealed by the experimental results with the addition of 20 % 2PN or 20 % 2M2BN.

3.2. Explanation of the inhibition effect

To further understand the inhibition effect, the relative energies of the eight nitriles and their X-NiL₂ complex have been determined by DFT calculations, as shown in Fig. 2. The reactant 2M3BN is selected as the reference, and the relative energies of 2PN and 2M2BN are negative because of the conjugation of C=C bond with C=N moiety. Thus, the formation of 2PN and 2M2BN is more favorable thermodynamically, especially for branched 2M2BN with the lowest energy. In contrast, 2M3BN and 3PN are non-conjugated isomers with a higher energy and show higher reactivity.

Next, the energies of all the detected nitriles combined with the NiL₄ catalyst, forming corresponding intermediates X-NiL₂ (X: nitriles), were

calculated. Using the energy of (2M3BN)NiL₂ as the reference, the calculated relative energies of X-NiL₂ are depicted in Fig. 2. The lowest energy of 2PN binding to the NiL₄ catalyst, which is -11.0 kcal/mol for (C2PN)NiL₂ and -13.1 kcal/mol for (T2PN)NiL₂, indicates that both C2PN and T2PN are preferentially bound to the NiL₄ catalyst to form the most stable intermediates (C2PN)NiL₂ and (T2PN)NiL₂. However, these intermediates are not reactive because no conversion of 2PN is detected when adding 2PN to the NiL₄ catalytic system at the same reaction conditions (see Supplementary material). Thus the decrease in catalytic activity in Fig. 1(d) could be attributed to the increased formation of the stable (2PN)NiL₂ intermediate. In addition, the most stable by-product 2M2BN could also bind to NiL₄ and produce the relatively stable (2M2BN)NiL₂ intermediate, which also decreased the catalytic activity (Fig. 1(c)). Similarly, no conversion of 2M2BN was detected when 2M2BN was added to the NiL₄ catalytic system (see Supplementary material). Because (2M2BN)NiL₂ had a higher energy than (2PN)NiL₂, 2PN showed a stronger inhibition effect on the catalytic activity than 2M2BN, which was consistent with the experimental results in Fig. 1.

Using the data shown in Fig. 1 (c) and (b), the quantitative relationship between the conversion of 2M3BN and the content of byproducts (2M2BN and 2PN) has been determined through multivariate regression (see *Supplementary material*), as shown in **Formula (1)**. Based



Fig. 2. The relative energies of nitriles and $X-NiL_2$ (X: nitriles). (No C3PN was detected in the isomerization reaction experiment.)



on this formula, the calculated conversion of commercially available 2M3BN (72.8 %) is 32.5 %, which is very close to the experimentally measured conversion (35.5 %). In addition, the quantitative relationship also provides useful insights for understanding the inhibiting effects. As 2M2BN and 2PN present in the isomerization of 2M3BN, 2M2BN and 2PN decrease the reaction rate constant (it is 1.4961 in **Formula (1)** when no 2M2BN and 2PN exist in reaction system) during the reaction, which means that the presence of 2M2BN and 2PN makes some catalyst lose their catalytic ability. Here, what needs to be explained is that **Formula 1** is only used to quantitatively predict the catalytic activity of the reaction system rather than the reaction kinetic equation.

$$\ln \frac{1}{1-X} = 1.4961 * e^{-0.04353^* x_{2M2BN} - 0.05964^* x_{2PN}}$$
(1)

X means the conversion of 2M3BN at 1 h, x_{2M2BN} and x_{2PN} represent the percentage content of 2M2BN and 2PN in the isomerization process, respectively.

Furthermore, under the same reaction conditions as used in Fig. 1(c) and (d), 0.65 mL 2M2BN was mixed with NiL₄ and stirred for 1 h at 100 □, then 3.23 mL 2M3BN was added so that the reaction system contained 20 % 2M2BN. The experimental results showed that the activity of NiL₄ sharply decreased, and the conversion of 2M3BN was only 18.6 % at 4 h while it was 83 % when 2M3BN including 20 % 2M2BN was used as reactant (Fig. 1(c)). For 2PN, 0.80 mL 2PN was mixed with NiL₄ and stirred for 1 h at 100 °C, then 3.26 mL 2M3BN was added to have 20 % 2PN in the reaction system for comparison, and the conversion of 2M3BN was 10.8 % at 4 h while it was 77.6 % using 2M3BN including 20 % 2PN as reactant as shown in Fig. 1(d). The decrease of reaction rate indicates that 2M2BN or 2PN can bind directly with the NiL₄ catalyst and form (2M2BN)NiL2 and (2PN)NiL2, respectively, when they are mixed with the catalyst. In addition, the inhibition on the catalytic activity is more noticeable as the NiL₄ catalyst is reused employing 72.8 % 2M3BN as reactant. In the second isomerization, 90 % conversion of 90 % 2M3BN was obtained at 4 h (Fig. 1(a)) while the conversion was only 45 % at 4 h using 72.8 % 2M3BN as reactant (Fig. 1(b)). The reason for a greater loss of activity showed in Fig. 1(b) was that more NiL₄ catalyst was combined with 2M2BN or 2PN in the reaction system. The lower conversion of 2M3BN in the above situations is that the active nickel is taken out of the productive catalytic cycle as dead-end intermediates ((2M2BN)NiL₂ and (2PN)NiL₂). Here, three types of the formation of the dead-end intermediates are proposed to understand the inhibiting effect in mechanistic insights, as shown in Scheme 2: (1) 2M2BN or 2PN directly combines with NiL₄ causing a lower catalytic activity; (2) at the beginning of the isomerization reaction, 2M3BN bound with the catalyst

is replaced by 2M2BN or 2PN, resulting in a catalytic inhibition; (3) at the end of the isomerization reaction, 2M2BN or 2PN replaces 3PN forming dead-end intermediates. Compared to the previous results on the deactivation caused by the formation of $Ni(CN)_2$ via the reaction of NiL_4 and HCN [3], other new ways accounting for the lower catalytic activity in the isomerization of 2M3BN are found in the current study. To improve the catalytic activity in the isomerization of 2M3BN, it is desired to increase the selectivity to 3PN to prevent the increase of 2M2BN and 2PN and suppress the combinations of 2M2BN and 2PN in 2M3BN with the NiL_4 catalyst.

3.3. Suppressing the inhibition effect

For catalytic isomerization of 2M3BN, the research on diphosphines indicates that the space a ligand occupies around the Ni center is an extremely important parameter for modulating the catalytic performance and the optimal steric congestion improves the catalyst activity [8]. With this in mind, a reasonable solution is explored to suppress the inhibition effect.

Several parameters have been proposed to quantify the steric congestion, such as the Tolman cone angle (θ) [15], solid angle (Ω) [32] and percent buried volume (%V_{bur}) [28,29]. To better describe the steric environment conferred on Ni center by ligands, the %V_{bur} was employed to calculate the percent of volume occupied by ligands around the Ni center and was used to assist the selection of suitable ligands, and the %V_{bur} of the intermediates X-NiL₂ in Fig. 2 are calculated. As shown in Table 1, (2M2BN)NiL₂ and (2PN)NiL₂ have bigger %V_{bur} value. This prompts us that rationally designing or regulating the steric congestion of the catalytic intermediate provides desirable method to inhibit the combination of these by-products with the NiL₄ catalyst. Therefore, the bulky ligands are used to prevent the internal coordination of 2M2BN or 2PN.

On the basis of the V_{bur} results, several ligands are selected, including mL, oL, dppe, dppp3, dppb, dppp5, dpph, dppf, Xantphos and XantN, and their structures are depicted in Table 2. In order to give a

Table 1

The %V _{Bur} o	f X-NiL ₂	(X:	nitriles). ^a
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Х	2M3BN	T2M2BN	C2M2BN	T2PN	C2PN	T3PN	4PN
%V _{Bur}	79.7	83.3	83.7	82.8	82.3	83.3	81.3

 $^{\rm a}\,$ Bondi radii scaled by 1.17, 4.0 Å for the sphere radius and the mesh spacing value s =0.1 Å.



Scheme 2. The ways of forming (2M2BN)NiL₂ and (2PN)NiL₂ intermediates.

Table	2
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The structure of ligands used and the %VBur value of (2M3BN)Ni(Ligand) intermediate.

Ligand	L	mL	oL	dppe	dppp3	dppb
Structure	\land	()	\bigcirc	$\bigcirc \bigcirc$	\bigcirc \bigcirc	\bigcirc \bigcirc
$\%V_{Bur}$ of partial substitution	°.,.°		o. _p .o			
	79.7	86.2	87.6	84.0	85.1	85.6
$\%V_{Bur}$ of total substitution	79.7	84.2	86.5	81.4	84.4	86.2
Ligand	dppp5	dpph	dppf	Xant	phos	XantN
Structure	\bigcirc \bigcirc	\bigcirc \land	PPh;	2		$\cap \cap$
$\%V_{Bur}$ of partial substitution			Fe PPh:		I IO	
	86.2	85.6	-	_		
$\% V_{Bur}$ of total substitution	87.5	89.3	85.2	87.2		87.6

larger value of $\%V_{bur}$, the formation of the new catalytic intermediates via partial or total substitution reactions is designed as these ligands are added to the NiL₄ system. Here, partial substitution means only one L in (2M3BN)NiL₂ is replaced by the added ligands while total substitution refers that both L are replaced. In order to clearly illustrate these two situations, the corresponding structures with dppp5 ligands are shown in Fig. 3. The $\%V_{bur}$ values of (2M3BN)Ni(Ligand) are used to evaluate the steric effect of the ligands. After the substitution reaction, the $\%V_{bur}$ of the catalytic intermediates increases from 79.7 % to 84.0–89.3 %. Under the circumstance of partial substitution, (2M3BN)NiL(mL) and (2M3BN)NiL(oL) provide bigger $\%V_{bur}$ (86.2 % and 87.6 %) while (2M3BN)NiL(diphosphine) gives close $\%V_{bur}$ values (dppe : 84.0 %, dppp3 : 85.1 %, dppb : 85.6 %, dppp5 : 86.2 %, and dpph : 85.6 %), as listed in Table 2. For total substitution, the increased $\%V_{bur}$ of (2M3BN)Ni(Ligand) are also observed.

To test the above strategy, the selected ligands are evaluated in the NiL₄ catalyzed isomerization reaction, and the results are shown in Fig. 4. Although the addition of L increased the selectivity to 90 % and thus hindered the formation of 2M2BN and 2PN, the excess ligand inhibited the dissociation of the L in NiL₄, resulting in a decrease in catalytic activity (area A in Fig. 4). Using extra mono-ligands (mL or oL) increased the selectivity to 3PN from 85 % to 92 %. Furthermore, the 3PN selectivity was 90 % when the Ni(mL)₄ was employed as catalyst. Recalling that the %V_{bur} increased from L (79.7 %) to oL (87.6 %), as listed in Table 2, the improvement in 3PN selectivity could be attributed to the increased steric effect. Further, diphosphines were added to the NiL₄ catalytic system to improve the catalytic activity. The results of the 2M3BN conversion and 3PN selectivity are shown in area B in Fig. 4. The NiL₄ catalyst with dppp5 ligand give a 92 % conversion of 2M3BN and >98 % selectivity to 3PN, which is the best result in this work. Compared with the experimental results using only the NiL₄ catalyst (Fig. 1(b)), adding dppp5 greatly improves the catalytic performance (the

conversion of 2M3BN : 74.5%-92% at 3 h, and the selectivity to 3PN : 90%-98%). However, adding dppe, dppf, Xantphos or XantN deceases the 2M3BN conversion from 82 % to below 40 % at 4 h of reaction (see Supplementary material). Diphosphines (dppf, Xantphos or XantN) with rigid backbone failed to meet the requirements for improving the catalyst performance. In addition, Ni(COD)₂ and ligands were used to simulate the total substitution experimentally, and the catalytic results were area C in Fig. 3, (2M3BN)Ni(dppp3), (2M3BN)Ni(dppb) and (2M3BN)Ni(dppp5) with the $\% V_{bur}$ of 84.8 %, 86.2 % and 87.5 %, respectively, provides 99 % selectivity to 3PN, but only (2M3BN)Ni (dppb) offeres a high conversion (93.4 %) of 2M3BN. However, As mentioned earlier, expensive Ni(COD)₂ limits its large-scale use. As for (2M3BN)Ni(dppe) and (2M3BN)Ni(dpph), a smaller (81.4 %) or larger (89.3 %) %V_{bur} value would provide the negative consequences (see Supplementary material). Therefore, a method for combining NiL₄ with dppp5 ligand to effectively improve the catalyst performance was discovered.

Moreover, using dppp5 and NiL₄ as the catalyst, the selectivity to 3PN could be maintained above 98 % when commercially available 72.8 % 2M3BN was added in 3 successive aliquots, and the catalytic activity moderately decreased from 90 % to 71 %, as shown in Fig. 1(e). The optimal experimental conditions (see *Supplementary material*) were determined as follows: reaction temperature of 110 °C and NiL₄ : dppp5 : 2M3BN = 1 : 1 : 30. The 2M3BN conversion could be further increased to 93.4 % at 3 h at the optimal conditions and the selectivity to 3PN maintained at 98 % in Fig. 1(f).

All our attempts to isolate (dppp5)NiL₂ have failed, to gain preliminary insights in the isomerization of 2M3BN, the mixture of NiL₄ and dppp5 in a 1 : 1 ratio was heated for 30 min at 100 °C and then analyzed by NMR. To better visualize the nickel species, NiL₄, L and the mixture of Ni(COD)₂ and dppp5 were also monitored by NMR. The ³¹P NMR spectrum were shown in Fig. 5. Chemical shifts of free P atoms in L and



Fig. 3. The structure of the (dppp5)NiL (left) and the Ni(dppp5) (right).



Fig. 4. The catalytic results using different ligands [a].

^[a] area **A** is the result of the isomerization reaction of using NiL₄ combined with monodentate phosphorus ligands (L, mL, and oL) as catalyst, area **B** is the result of the isomerization reaction of using NiL₄ and bidentate phosphine ligands (dppp3, dppb, dppp5, and dpph) as a catalyst, and area **C** is the result of using Ni(COD)₂ and the bidentate phosphines (dppp3, dppb, dppp5, and dpph) as catalyst in the catalyzed isomerization reaction.



Fig. 6. The catalytic kinetics using NiL₄ and dppp5 as catalyst.

Therefore, a first-order reaction means that the reaction is not catalyzed by Ni(dppp5) (in Fig. 3). According to the NMR and in-situ IR results, the improved result in Fig. 1(f) could be attributed to the formation of (dppp5)NiL₂.

3.4. The crystal structure

The crystal of the (dppp5)Ni(CN) species suitable for single-crystal Xray diffraction studies were obtained from the reacted system by vapor diffusion using the hexane and cumene system. As shown in Fig. 7, the structure of the (dppp5)Ni(CN) species depicts that the nickel atom is in a planar configuration and is attached to four groups: two CN groups and two P atoms in different dppp5 ligands. The parameters of the crystal can be found in *Supplementary material*.

Although the combination of 2M2BN and 2PN with the nickel catalyst is suppressed with the coexistence of NiL₄ and ligand dppp5, the catalytic activity still decreases gradually under optimal conditions. The conversion of 2M3BN is 65 %, 55.4 % and 43 % for the first, second and third times at 1 h, respectively, as shown in Fig. 1(e). When (dppp5)Ni (CN) is used as the catalyst to further investigate this phenomenon, no activity is found in the isomerization reaction. (dppp5)Ni(CN) accounts for the decrease of the catalytic activity in Fig. 1(e).

4. Conclusions

In summary, the current study reports the inhibition effect of 2PN



dppp5 were observed at 128.15 ppm and -13.50 ppm, respectively. The signal at 130.40 ppm was assigned to the NiL₄ complex. A new signal at 24.52 ppm indicated that only one phosphorus atom in dppp5 was linked to nickel while the sharp signal appeared at 31.78 ppm when both phosphorus atoms in dppp5 were coordinated to the nickel atom (see Ni (dppp5) in Fig. 3). Based on the peak area (see *Supplementary material*), the nickel atom linked to one phosphorus atom in dppp5 was combined with two L to form (dppp5)NiL₂.

To study the changes of the NiL₄ catalyst after adding dppp5 in the catalytic process, the kinetics of the 2M3BN isomerization was studied by ReactIR¹⁵ (more details in *Supplementary material*). The results showed that the reaction was first order with respect to 2M3BN, as shown in Fig. 6. The calculated reaction rate constant (*k*) was 1.232 h⁻¹ for 2M3BN and 1.211 h⁻¹ for 3PN, indicating that the selectivity to 3PN is 98.3 %. As previously reported that when Ni(dppp5) was used as catalyst, the isomerization reaction followed a zero-order kinetics [8].



Fig. 7. The crystal structures of (dppp5)Ni(CN) species.

and 2M2BN on the catalytic activity in the isomerization of 2M3BN and provides an effective method to weaken the inhibition effect. The quantitative relationship shows that 2PN and 2M2BN in the feedstock are detrimental to the catalytic activity, and their inhibition effect is elucidated by experimental studies and DFT calculations. The generation of the dead-end intermediates (2PN)NiL₂ and (2M2BN)NiL₂ makes nickel atom out of the productive catalytic cycle in the isomerization process, which decreases the catalytic activity. Therefore, it is desired to suppress the inhibition effect of 2PN and 2M2BN by rational catalyst design. This is realized by increasing the steric effect of the catalytic intermediates with the addition of dppp5 to the NiL₄ catalytic system to prevent 2PN and 2M2BN from binding to the catalyst. This simple approach operation provides improved conversion of 2M3BN (75.4 %-93.4 %) and excellent selectivity to 3PN (90 %-98 %). Undoubtedly, using the NiL₄ combined with dppp5 is a better choice for the DuPont process. Finally, based on the steric effect, a method for combining NiL₄ with other phosphine ligands to effectively improve the catalyst performance is discovered. This method is suitable for any ligand, and greatly accelerates the efficiency of ligand screening. In order to further improve the conversion of 2M3BN in the isomerization process, more ligands will be screened in our next research.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.mcat.2020.111259.

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K. Liu et al.

Molecular Catalysis 498 (2020) 111259

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