

Short communication

Green synthesis of low-carbon chain nitroalkanes via a novel tandem reaction of ketones catalyzed by TS-1

Qingyan Chu^{a,b}, Guangke He^{a,*}, Yang Xi^a, Ping Wang^{a,c}, Haoxuan Yu^c, Rui Liu^a, Hongjun Zhu^{a,*}^a College of Chemistry and Molecular Engineering, Nanjing Tech University, Nanjing 211816, China^b Research institute of QILU petrochemical company, SINOPEC, Zibo 255400, China^c School of Chemical Engineering, Shandong University of Technology, Zibo 255049, China

ARTICLE INFO

Keywords:

TS-1
Catalyzed oxidation
Tandem reaction
Nitroalkanes
Green synthesis

ABSTRACT

A green and efficient one-pot method has been developed for the synthesis of low-carbon chain nitroalkanes via a novel TS-1 catalyzed tandem oxidation of ketones with H₂O₂ and NH₃. The tandem reaction including amoxidation, oximation and oxidation of oximes, afforded up to 88% yield and 98% chemo-selectivity requiring only 90 min, at 70 °C and atmospheric pressure. Moreover, this method was even amenable to 100-fold scale-up without loss of chemical efficiency with 87% yield, represents a significant advance towards industrial production of nitroalkanes. Furthermore, the plausible mechanism of TS-1 catalyzed tandem oxidation of ketones to prepare nitroalkanes was proposed.

1. Introduction

As important fine chemicals, nitroalkanes are widely used as solvents and fuels, and also to prepare explosives, dyes, plastics, perfumes, pesticides, pharmaceuticals and more [1,2]. At present, nitroalkanes are usually obtained through the following several methods: a) substitution reaction of alkyl halides with nitrites [3,4]; b) direct nitration of alkanes with nitric acid or NO₂ [5,6]; c) oxidation of alkylamines by KMnO₄ [7], NaWO₄·2H₂O-H₂O₂ [8], dimethylperoxy ketone [9] or methyltrioxorhenium-H₂O₂ [10]; d) oxidation of oximes by peroxytrifluoroacetic acid [11], Mo(VI) oxodiperoxo complex [12], sodium perborate [13], and other oxidants [14]. Some of the above-mentioned synthetic methods required special safety precaution and caused troublesome disposal of spent liquors, and some of them proceed in aqueous media which can easily lead to partial hydrolysis of oximes and low catalyst turnover numbers (TONs) that enable the work up of the mixtures a tedious process. In 2006, Rozen, S. reported the oxidation of azides and amino compounds [15–17]. However, the HOF-CH₃CN oxidant required hazardous fluorine gas for the preparation; also, this reagent is quite unstable and needs to be prepared in situ. Therefore, it is necessary to develop a simple, efficient and environmentally benign industrial route to nitroalkanes. In the past few years, Titanium Silicate-1 (TS-1) catalyst with Mobil Five (MFI) type structure has been widely used in H₂O₂ oxidation system [18,19]. Although TS-1 exhibits good catalytic activity towards amoxidation of ketones to corresponding oximes, small amounts of nitroalkanes (1.3–5.8%) still exist in the

system due to deep oxidation of oximes [20–22]. We proposed that nitroalkanes were mainly originated from the further oxidation of oximes with H₂O₂ through the catalysis of TS-1. Furthermore, the side reaction we considered before has been verified and optimized as a main reaction. Finally, a novel tandem reaction of ketones catalyzed by TS-1 was found and applied in synthesis of nitroalkanes from ketones.

In this paper, a variety of structurally diverse oximes catalyzed oxidation were investigated in terms of reaction conditions and catalyst in detail, and encouraging experimental results were obtained. On this basis, a novel tandem reaction of direct green synthesis of nitroalkanes from ketones by TS-1 catalyzed with H₂O₂ and NH₃ was achieved.

2. Experimental

2.1. Catalyst preparation and characterization

All chemicals were analytical grade and used as received. TS-1 catalyst was prepared by a hydrothermal method (the preparation process was described in Supplementary material) [23]. The prepared catalyst was characterized by X-Ray Fluorescence Spectrometer (XRF), Scanning electron microscopy (SEM), transmission electron microscope (TEM), the Fourier transform infrared (FT-IR), X-ray diffraction (XRD), N₂ adsorption, X-ray photoelectron spectroscopy (XPS) and FT-IR spectroscopies of pyridine adsorption (Py-IR). The analysis conditions had been detailed in Supplementary material 1.

* Corresponding authors.

E-mail addresses: hegk@njtech.edu.cn (G. He), zhu hj@njtech.edu.cn (H. Zhu).

2.2. Synthesis of nitroalkanes

TS-1 catalyzed oxidation of ketones or oximes to prepare nitroalkanes was carried out in a reaction vessel. A solution of ketones or oximes, TS-1 catalyst and $\text{NH}_3\cdot\text{H}_2\text{O}$ in MeOH was mixed and heated at 70 °C. To this mixture was slowly injected H_2O_2 by a peristaltic pump within 30 min. After stirring for an additional 1 h, the progress of the reaction was monitored by Agilent 7820A GC System. Upon completion, the resulting mixture was cooled to r.t. and TS-1 catalyst filtered off. Then, saturated NaHSO_3 aqueous solution was added to deal with the unreacted H_2O_2 . After removing MeOH by distillation, the residual aqueous phase was extracted with DCM. The combined organic layer was concentrated in vacuum to give the nitroalkanes. All reactions were performed in reaction vessels at atmospheric pressure.

3. Results and discussion

3.1. Catalyst characterization

The morphology analysis of TS-1 was shown in Fig. S1. It is observed that the well-defined, uniform cubic crystallites are distributed homogeneously with particle size of about $1.1 \times 0.64 \times 0.24 \mu\text{m}$ in the SEM (Fig. S1a) and TEM images (Fig. S1b). And the lattice structures of TS-1 can be well distinguished from the TEM images (Fig. S1c and S1d). Moreover, the clear lattice fringes with two spacing intervals (1.1 nm and 0.36 nm) correspond to the crystallographic planes of monoclinic TS-1, which are in well accord with XRD (Fig. S3) peaks of 7.8° and 24.4°. To gain insights into the distribution of TS-1, elemental mappings were taken (Fig. S1e). It could be seen that the three elements of Ti, Si and O were evenly distributed in the prepared catalytic material. Furthermore, the XRF analysis showed that the Si/Ti molar ratio of the TS-1 was 38.

The FT-IR spectrum of TS-1 sample showed that an obvious IR absorption peak at 983 cm^{-1} (Fig. S2), indicating the collective vibration of Si-O-Ti or Si-O bond influenced by Ti(IV) of TS-1 framework [24]. The results confirmed that titanium was present in the TS-1 framework [25]. The XRD peaks at $2\theta = 7.8^\circ, 8.8^\circ, 23.2^\circ, 23.8^\circ$ and 24.3° showed the MFI topological structure of TS-1 (Fig. S3) [26]. And the diffraction peak at $2\theta = 25.3^\circ$ was not observed, which confirmed that anatase TiO_2 is not formed in TS-1 [27].

As shown in the N_2 adsorption-desorption isotherms (Fig. S4), the adsorption isotherm coincided well with the desorption isotherm from relative pressure values between 0 and 0.47, indicating that the presence of micropores. A hysteresis loop was clearly observed from relative pressures of 0.5 to 1.0, which showed the presence of mesopores. And the upward tail of the N_2 adsorption-desorption isotherm showed the presence of macropores. The formation of mesopores and macropores is caused by TS-1 stacking. Further, TS-1's BET specific surface area, pore volume, and pore size are $328.23 \text{ m}^2/\text{g}$, $0.19 \text{ cm}^3/\text{g}$ and 2.29 nm, respectively.

The Py-IR spectra (Fig. 1) were employed to evaluate the types and strength of Brönsted and Lewis acid sites on the surface of prepared TS-1 [28,29]. The bands of 1446 and 1604 cm^{-1} , and the bands at 1544 and 1639 cm^{-1} demonstrated the existence of Lewis acid and Brönsted acid sites, respectively. And the band at 1489 cm^{-1} was a combination between two separate bands at 1446 and 1544 cm^{-1} . In addition, the changes of Brönsted and Lewis acidity were also observed at different desorption temperatures (150, 250, 350 and 450 °C). As shown in Fig. 1, the Brönsted acidity reduced more rapidly than the Lewis acidity with the temperature rising, which indicated the acidic sites of Lewis acidity are more than that of Brönsted acidity in TS-1 catalyst.

As shown in Fig. S5a, the binding energy values of $\text{Ti } 2p_{3/2}$ and $2p_{1/2}$ were observed at 458.5 and 465.0 eV, respectively. And a 6.5 eV splitting from $\text{Ti } 2p_{3/2}$ to $\text{Ti } 2p_{1/2}$ in the XPS spectrum indicated that all titanium as octahedron Ti^{4+} existed in the TS-1 [30,31]. The binding energy value of Si $2p$ was also observed at 103.4 eV, which indicated

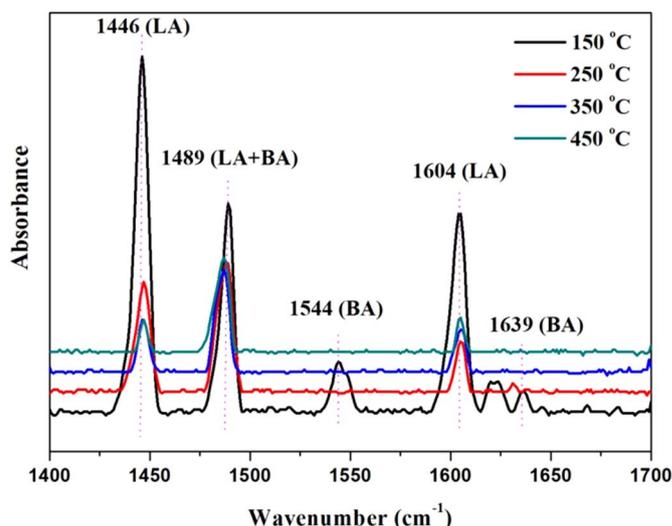


Fig. 1. Py-IR spectra of TS-1.

that Si existed in the TS-1 (Fig. S5b).

3.2. Synthesis of nitroalkanes from oximes

Next, we tested the reactivity of TS-1 through the oxidation of *n*-butanaloxime (1a) with H_2O_2 in the presence of $\text{NH}_3\cdot\text{H}_2\text{O}$ at 70 °C (Table 1). The experimental results showed that the amount of TS-1 had an important effect on the reaction. When 25 mg of TS-1 was used, the reaction afforded the 1-nitrobutane (2a) in only less than 10% yield with the 1:1 ratio of 2a/3a. And the yield could be dramatically increased to 96% by adding 100 mg of TS-1 to the reaction (entry 3). In fact, lowering the reaction temperature caused lower conversion rate and inferior selectivity (entries 4–5). However, increasing the concentration of H_2O_2 or reducing its amount did not maintain a satisfactory result (entries 6–8). Solvents screening experiments indicated that MeOH was a better reaction medium than EtOH, *i*-PrOH, *t*-BuOH, and MeCN (entry 3 vs. entries 9–12). No reaction occurred in the absence of catalyst (entry 13). Thus, the reaction efficiently proceeded when 100 mg of TS-1 was used in combination with H_2O_2 (2.0 equiv.) in MeOH at 70 °C (entry 3).

Having established the standard conditions for the TS-1 catalyzed oxidative nitration (Table 1, entry 3), we next moved to the scope and limitation studies using a variety of structurally diverse oximes (Table 2). The reactions of acetaldoxime, propionaldoxime, and *n*-pentaldoxime with H_2O_2 proceeded smoothly and afforded the corresponding 1-nitroalkanes in 83% to 97% yields with excellent selectivities (entries 2–4). However, the oxidation reactivity dropped sharply with an increase of the carbon chain length of oximes (entries 5–6), and the reaction did not even work at all for decanaloxime (entry 7). This was probably caused by the steric hindrance of substrates impeding the interaction of oximes with the active sites of TS-1. Unexpectedly, acetoxime (1 h) could also be oxidized to 2-nitropropane in 91% yield with 93/7 selectivity under the standard conditions (entry 8). Similarly, the yield and selectivity of the TS-1 catalyzed oxidation markedly decreased with the increase of the steric hindrance from alkyl group on ketone oximes (entries 9–11).

3.3. Synthesis of nitroalkanes from aldehydes/ketones

Inspired by the oxidative results of oximes, we speculated whether low-carbon aldehydes and ketones could also be directly oxidized to corresponding nitroalkanes by the protocol. After many modifications to the established standard conditions, we still could not observe the oxidation from *n*-butanal to 1-nitrobutane in the presence of H_2O_2 and

Table 1
Optimization of reaction parameters for the TS-1 catalyzed oxidation of *n*-butanaloxime with H₂O₂.^a

Entry	TS-1 (mg)	H ₂ O ₂ (equiv.)	Solvent	GC yield of 2a(%) ^b	Ratio of 2a/3a (%) ^b
1	25	2	MeOH	5	50:50
2	50	2	MeOH	42	83:17
3	100	2	MeOH	96	97:3
4 ^c	100	2	MeOH	69	91:9
5 ^d	100	2	MeOH	58	90.5:9.5
6	100	2 ^e	MeOH	42	95:5
7	100	1.5	MeOH	96	96.5:3.5
8	100	1.25	MeOH	82	93:7
9	100	2	EtOH	47	88:12
10	100	2	<i>i</i> -PrOH	94	87:13
11	100	2	<i>t</i> -BuOH	66	89:11
12	100	2	MeCN	78	80.5:19.5
13	–	2	MeOH	0	–

^a Reaction conditions: *n*-butanaloxime (0.87 g, 10 mmol), MeOH (3.8 ml), H₂O₂ (30 wt%) and NH₃·H₂O (0.15 mmol, 26.5 wt%) reacted at 70 °C.

^b The yield and selectivity of the reaction were determined by GC analysis.

^c The reaction was conducted at 60 °C.

^d The reaction was conducted at 65 °C.

^e H₂O₂ (50 wt%) was used.

Table 2
Scope of TS-1 catalyzed oxidation of oximes with H₂O₂.^a

Entry	R ¹	R ²	GC yield of 2 (%)	Ratio of 2/3/4 (%)
1	<i>n</i> -C ₃ H ₇ (1a)	H	96 (2a)	97:3:0
2	Me (1b)	H	97 (2b)	98:2:0
3	<i>n</i> -C ₂ H ₅ (1c)	H	97 (2c)	97.5:2.5:0
4	<i>n</i> -C ₄ H ₉ (1d)	H	83 (2d)	96:4:0
5	<i>n</i> -C ₅ H ₁₁ (1e)	H	21 (2e)	92:8:0
6	<i>n</i> -C ₆ H ₁₃ (1f)	H	5 (2f)	91:9:0
7	<i>n</i> -C ₉ H ₁₉ (1g)	H	0 (2g)	–
8 ^b	Me (1h)	Me	91(2h)	93:0:7
9 ^b	Me (1i)	Et	35 (2i)	53.5:0:46.5
10 ^b	Me (1j)	<i>n</i> -C ₃ H ₇	12 (2j)	48:0:52
11 ^b	Et (1k)	Et	1(2k)	7.5:0:92.5

^a Reaction conditions: 1 (10 mmol), TS-1 (0.10 g), MeOH (3.8 ml), H₂O₂ (2.0 equiv., 30 wt%), and NH₃·H₂O (0.15 equiv., 26.5 wt%) reacted in methanol at 70 °C.

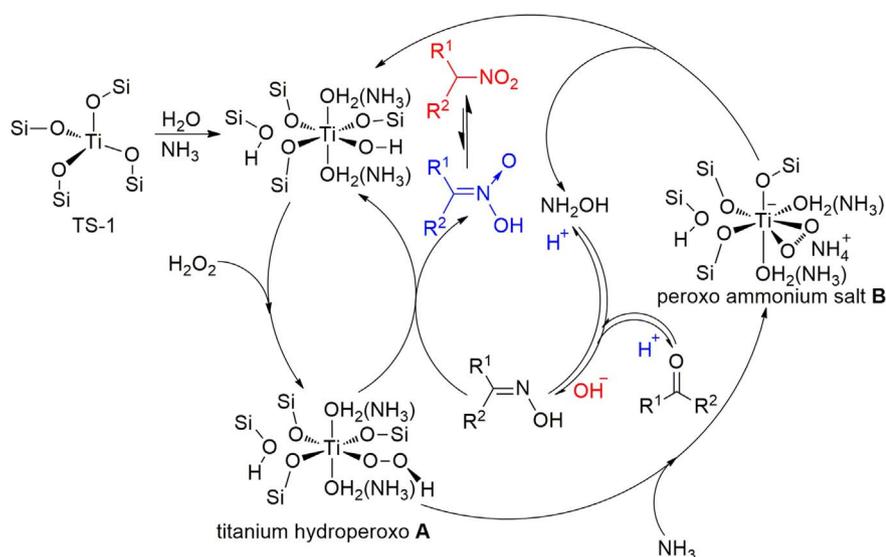
^b NH₃·H₂O (0.45 equiv., 26.5 wt%) was added.

Table 3
The synthesis of nitroalkanes in tandem reaction via TS-1 catalyzed direct oxidation of aldehyde/ketone with H₂O₂.^a

Entry	R ¹	R ²	GC yield of 2 (%)	Ratio of 2/1 (%)
1	Me (4b)	Me	88 (2h)	98:2
2	Et (4c)	Me	68 (2i)	76:24
3	<i>n</i> -C ₃ H ₇ (4d)	Me	Complicated	–
4	<i>n</i> -C ₃ H ₇ (4a)	H	0 (2a)	0:100 ^b

^a Reaction conditions: 4 (62.5 mmol), TS-1 (0.625 g), MeOH (20.5 ml), H₂O₂ (1.2 equiv., 30 wt%), and NH₃·H₂O (1.5 equiv., 26.5 wt%) reacted in MeOH at 70 °C.

^b Butyric acid instead of *n*-butanaloxime was formed.



Scheme 1. Proposed mechanism of TS-1 catalyzed tandem oxidation of ketones.

$\text{NH}_3\cdot\text{H}_2\text{O}$ (Table 3, entry 4), but found that the conversion to *n*-butanoic acid was nearly completed, which indicated that the latter path was more favourable than the former one energetically. Fortunately, when acetone (**4b**) was subjected to the TS-1 catalyzed system, we could achieve the moderate conversion rate (88%) and good selectivity (98/2) by appropriately adjusting the amount of $\text{NH}_3\cdot\text{H}_2\text{O}$ and H_2O_2 (entry 1). It should be noted that and the product 2-nitropropane (**2h**) was achieved only as the main by-product in similar TS-1 catalyzed oxidative systems [21,22]. For 2-butanone, the moderate yield (68%) and selectivity (76/24) were obtained (entry 2). However, the TS-1 catalyzed oxidation of 2-pentanone became complicated under the identical conditions (entry 3). Considering TS-1 is a kind of microporous Ti–Si molecular sieve with MFI structure, and Ti^{4+} active center is located in the pore of molecular sieve, it is difficult for macromolecules to enter the pore to react on the active sites. So the TS-1 catalyzed oxidation of macromolecular ketones (such as cyclohexanone [32]) would be stopped at the stage of ketone oximes.

3.4. Proposed mechanism of the catalytic reaction

According to literature reports [33,34] and our experimental results, we proposed the plausible mechanism of the tandem reaction through the ammoxidation, oximation and oxidation of oximes sequence (Scheme 1): Initially, the main Ti^{4+} active center of Ti–Si molecular sieve combines with H_2O and NH_3 molecules into six-fold coordinated Ti(IV) complex, forming the titanium hydroperoxo intermediate **A** under the oxidation of H_2O_2 . Then, the intermediate **A** reacted with ammonia to produce the peroxo ammonium salt **B**, which would easily release NH_2OH via ammoxidation and regenerate TS-1·2 H_2O [33]. Finally, the oximes, derived from the nucleophilic addition-elimination of NH_2OH with ketones, would transform into their oxides under the co-oxidation of intermediate **A** with H_2O_2 , and finally produced the nitro compounds via tautomerism [10]. In short, the three-step tandem reaction formed a catalytic cycle, which includes the ammoxidation, oximation and oxidation of oximes in a single pot.

3.5. Scale-up experiments and reusability of catalyst

In fact, this oxidative process was not limited to the small scale (10 mmol), as a scale-up (1 mol) reaction of either acetone or acetone oxime to produce 2-nitropropane **2h** could be conveniently performed with the isolated yield of 87% (Supplementary material 3), which paved the way for industrial production. And 2-nitroalkanes can also be conveniently used to the preparation of amino alcohols, such as the

environmental protection paint 2-amino-2-methylpropanol (AMP-95), which was not easily commercially available due to the shortage of 2-nitropropane.

In addition, five runs were tested in order to evaluate the recyclability of catalyst (Fig. S6). A slow decline in yields was observed after five runs for TS-1 catalyzed oxidation of acetone. However, the yield still remained ~61%. And the activity of used TS-1 for five times can be restored to 97%, compared to that of fresh catalyst by calcining regeneration at 550 °C for 6 h. The reason for the decrease of catalytic activity after recyclable use was mainly the carbon deposition.

4. Conclusion

In conclusion, TS-1 catalyst with low Ti/Si ratio was synthesized, characterized and applied to the catalytic synthesis of low-carbon nitroalkanes via a novel tandem reaction. The green synthesis was conducted from the direct oxidation of ketones at the presence of H_2O_2 and NH_3 under mild conditions, which produced up to 88% yield and 98% chemo-selectivity. Meanwhile, catalyzed oxidation reaction of oximes to nitroalkanes via TS-1 also gave a yield of 97% and a chemo-selectivity of 98%. Importantly, this method was successfully scaled up with excellent yield and selectivity, and represented a significant advance towards industrial production of nitroalkanes. Furthermore, a supposed mechanism of the TS-1 catalyzed oxidation of ketones or oximes to prepare nitroalkanes was proposed. To sum up, this new technique exhibits excellent atom economy, environment-friendly and prospective application in both academic and industrial fields.

Acknowledgement

The authors thank greatly the National Key Research and Development Program of China (2016YFB0301703), and the Natural Science Foundation of Jiangsu province, China (Grant No. BK20140937).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.catcom.2018.01.022>.

References

- [1] V.V. Patil, G.S. Shankarling, J. Organomet. Chem. 80 (2015) 7876–7883.
- [2] N. Ono, The Nitro Group in Organic Synthesis, Wiley, VCH, New York, 2001.
- [3] R. Ballini, L. Barboni, A. Palmieri, Green Chem. 10 (2008) 1004–1006.

- [4] M. Sawant, D.M. Trauth, J.G. Pendergast, US Pat. 20110092749, 2013.
- [5] G.G. Bachman, L. Kohn, *J. Organomet. Chem.* 17 (1952) 942–954.
- [6] Y. Nishiwaki, S. Sakaguchi, Y. Ishii, *J. Organomet. Chem.* 67 (2002) 5663–5668.
- [7] N. Kornblum, R.J. Clutter, W.J. Jones, *J. Am. Chem. Soc.* 78 (1956) 4003–4004.
- [8] J.C. Stowell, *J. Organomet. Chem.* 36 (1971) 3055–3066.
- [9] R.W. Murray, R. Jeyaraman, L. Mohan, *Tetrahedron Lett.* 27 (1986) 2335–2336.
- [10] R.W. Murray, K. Iyanar, J. Chen, J.T. Wearing, *Tetrahedron Lett.* 37 (1996) 805–808.
- [11] W.D. Emmons, A.S. Pagano, *J. Am. Chem. Soc.* 77 (1955) 4557–4559.
- [12] F.P. Ballistreri, E. Barbuzzì, G.A. Tomaselli, R.M. Toscano, *Synlett* (1996) 1093–1094.
- [13] G.A. Olah, P. Ramaiah, C.S. Lee, G.K.S. Prakash, *Synlett* (1992) 337–339.
- [14] D.S. Base, G. Vanajatha, *Synth. Commun.* 30 (1998) 4531–4535.
- [15] M. Carmeli, S. Rozen, *J. Organomet. Chem.* 71 (2006) 4585–4589.
- [16] M. Kol, S. Rozen, *J. Chem. Soc. Chem. Commun.* (1991) 567–568.
- [17] S. Rozen, M. Kol, *J. Organomet. Chem.* 57 (1992) 7342–7344.
- [18] S. Park, K.M. Cho, M.H. Youn, J.G. Seo, J.C. Jung, S. Baek, *Catal. Commun.* 9 (2008) 2485–2488.
- [19] Y. Zhang, C. Xia, M. Lin, Q. Duan, B. Zhu, X. Peng, B. Wang, S. Yuan, Y. Liu, X. Shu, *Catal. Commun.* 101 (2017) 1–4.
- [20] Q. Chu, P. Wang, G. He, M. Li, H. Zhu, R. Liu, F. Pei, *Chem. Eng. J.* 325 (2017) 169–175.
- [21] Z. Zhuo, W. Lei, X. Zhang, L. Wu, Y. Liu, M. He, *J. Catal.* 329 (2015) 107–118.
- [22] F. Song, Y. Liu, L. Wang, H. Zhang, M. He, P. Wu, *Appl. Catal. A Gen.* 327 (2007) 22–31.
- [23] M. Liu, X. Ye, Y. Liu, X. Wang, Y. Wen, H. Sun, B. Li, *Ind. Eng. Chem. Res.* 54 (2015) 5416–5426.
- [24] Y. Hasegawa, A. Ayame, *Catal. Today* 71 (2001) 177–187.
- [25] L.D. Pozzo, G. Fornasari, T. Monti, *Catal. Commun.* 3 (2002) 369–375.
- [26] R. Millini, E.P. Massara, G. Perego, G. Bellussi, *J. Catal.* 137 (1992) 497–503.
- [27] Q. Du, Y. Guo, H. Duan, H. Li, Y. Chen, H. Liu, *Fuel* 188 (2017) 232–238.
- [28] X. Ma, H. Guo, S. Wang, Y. Sun, *Fuel Process. Technol.* 83 (2003) 275–286.
- [29] R. Ediati, M. Ulfa, H. Fansuri, Z. Ramli, H. Nur, D. Prasetyoko, *J. Math. Fund. Sci.* 46 (2014) 76–90.
- [30] G.N. Vayssilov, *Catal. Rev.* 39 (1997) 209–251.
- [31] X. Gao, J. An, J. Gu, L. Li, Y. Li, *Microporous Mesoporous Mater.* 239 (2017) 381–389.
- [32] C. Dong, K. Wang, J.S. Zhang, G.S. Luo, *Chem. Eng. Sci.* 126 (2015) 633–640.
- [33] A. Zecchina, S. Bordiga, C. Lamberti, G. Ricchiardi, C. Lamberti, G. Ricchiardi, D. Scarano, G. Petrini, G. Leofanti, M. Mantegazza, *Catal. Today* 32 (1996) 97–106.
- [34] G. Tozzola, M.A. Mantegazza, G. Ranghino, G. Petrini, S. Bordiga, G. Ricchiardi, C. Lamberti, R. Zulian, A. Zecchina, *J. Catal.* 179 (1998) 64–71.