



Conversion of methanol over H-ZSM-22: The reaction mechanism and deactivation[☆]

Jinzhe Li, Yingxu Wei, Yue Qi, Peng Tian, Bing Li, Yanli He, Fuxiang Chang, Xinde Sun, Zhongmin Liu^{*}

National Engineering Laboratory for Methanol to Olefins, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian 116023, PR China

ARTICLE INFO

Article history:

Received 1 July 2010

Received in revised form 21 October 2010

Accepted 21 October 2010

Available online 4 December 2010

Keywords:

ZSM-22

Methanol

Methylation

Propene

Ethene

MTO

ABSTRACT

Conversion of methanol to olefins (MTO) over H-ZSM-22 was carried out in the pulse and the continuous-flow reaction systems. ¹³C labeling technique was used to reveal the reaction mechanism. The materials retained in the deactivated catalyst were detected by GC–MS after dissolving the catalyst framework and then extracting the organic species. The adsorption of these materials in ZSM-22 channels was computationally modeled. The results showed that the olefin methylation–cracking mechanism is the main route for the conversion of methanol over H-ZSM-22. It was suggested that the blockage of the zeolite pore openings by the coke species might be the reason of the relatively rapid deactivation of H-ZSM-22, instead of the prohibition of the formation of large transition-state intermediates involved in hydrocarbon pool mechanism.

© 2010 Elsevier B.V. All rights reserved.

1. Introduction

Methanol is an important platform product of coal chemistry. Light olefins can be obtained by conversion of methanol over acidic zeolite catalysts through the process known as MTO (methanol-to-olefins). Considerable effort has been devoted to the optimization of the catalyst performance and process conditions [1–3]. In parallel with that, numerous research works have been done to elucidate the reaction mechanism of MTO conversion [4–7] and more than 20 mechanisms have been proposed by different researchers [1]. Among the proposed mechanisms, the hydrocarbon pool mechanism attracted much more attention, which is an indirect mechanism and first proposed by Kolboe and co-workers based on the experiments of the MTO conversion over SAPO-34 [8–10]. According to the hydrocarbon pool mechanism, the reaction cycle involved the methylation of “hydrocarbon pool intermediates” confined in the cages of SAPO-34 by methanol and subsequent elimination of ethylene, propene, and butenes from the intermediates. Later, detailed studies revealed that the polymethylbenzenes composed largest part of the materials retained in the catalyst and that hexamethylbenzene was the most active species for methanol to olefin conversion [11–13]. Haw et al. proposed that the conversion of methanol over ZSM-5 also follows the hydro-

carbon pool mechanism [14,15], which was supported by Hunger and co-workers [16,17]. Furthermore, Cui et al. [18] reported that the MTO conversion could only take place on zeolites that allow the hydrocarbon pool mechanism to work, and that due to the transition-state shape selectivity, MTO conversion over ZSM-22 (a zeolite which has one-dimensional channel with 10-member ring opening) could only produce dimethylether as the product. They also found that ZSM-22 displayed a low but appreciable production of olefins at the beginning of methanol conversion, but they believed that it was the result of the impurity phase (ZSM-11) and/or the external acid sites [18].

However, Svelle and Bjorgen [19,20] pointed out that over ZSM-5, ethene and propene maybe produced through dual-cyclic reaction route. Ethene was formed through the hydrocarbon pool mechanism with lower methylated benzene as reactive intermediates, and apart from that, the olefin methylation–cracking cycle was also an effective route for the formation of propene, butenes and higher olefins. This suggests that if the reactions following the hydrocarbon pool mechanism were suppressed, methanol might be converted into olefins through the methylation–cracking route. In fact, our previous work presents a positive result of methylation–cracking route in methanol conversion over ZSM-22. Nearly complete conversion of methanol could be obtained over ZSM-22 at 450 °C (WHSV = 10 h⁻¹) [21]. In a very recent report from the group of Olsbye [22], they also found that under suitable conditions ZSM-22 has a conversion capacity comparable to that of SAPO-34. These results have been somewhat contradictive with the report of Cui et al. [18].

[☆] Student Award Paper.

^{*} Corresponding author. Tel.: +86 411 84685510; fax: +86 411 84691570.

E-mail address: liuzm@dicp.ac.cn (Z. Liu).

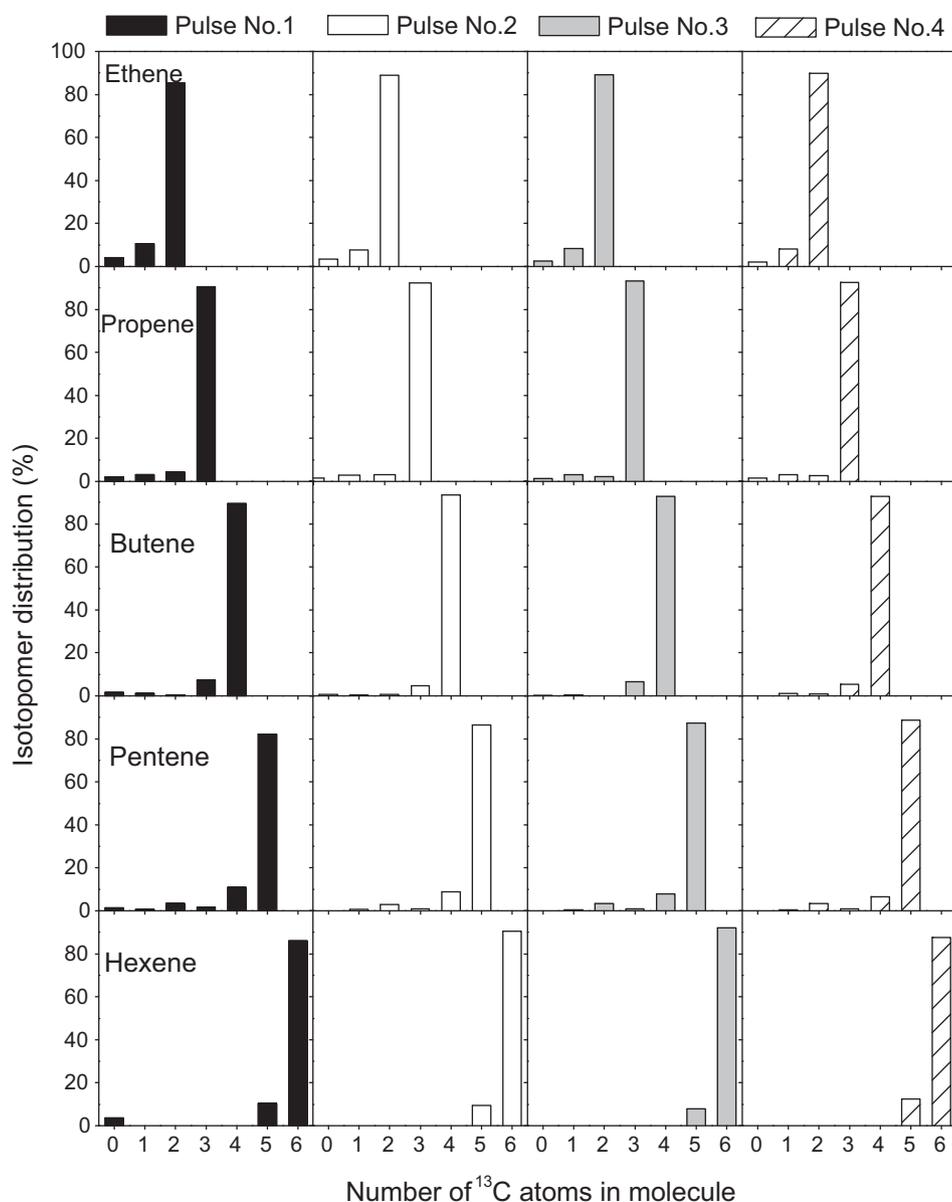


Fig. 1. Isotopic distribution in the effluent products of successive ¹³C-methanol pulse reaction over ZSM-22 at 450 °C after the pre-reaction of 15 pulses of ¹²C-methanol, CT=0.08 s.

In the present study, methanol conversion over ZSM-22 was carried out in the pulse and continuous-flow reaction systems. The reaction mechanism over ZSM-22 was elucidated by the aid of ¹³C labeling technique. It was demonstrated that the methanol could be converted into olefins over ZSM-22 through olefin methylation and cracking route. The blockage of the channel openings by coke species was proved to be the main reason for the low efficiency of methanol conversion over ZSM-22, instead of the prohibition of hydrocarbon pool species formation associated with the transition-state shape selectivity.

2. Experimental

2.1. Catalyst preparation and characterization

The sample of ZSM-22 (SiO₂/Al₂O₃ = 69) was kindly provided by another research group of Dalian Institute of Chemical Physics. The NH₄-ZSM-22 was obtained by ion-exchanging the calcined solid with the solution of ammonium nitrate. After the ion-exchange,

the sample was washed with deionized water, dried at 110 °C and finally calcined at 550 °C for 4 h to achieve H-ZSM-22.

The crystallinity and phase purity of the samples was characterized by powder X-ray diffraction (RIGAKU D/max-rb powder diffractometer) with Cu K_α radiation.

The acidity of the catalysts was determined by temperature programmed desorption of ammonia (NH₃-TPD). A catalyst sample of 0.14 g was loaded into a U-shaped micro-reactor and pre-treated at 650 °C for 30 min in a flow of helium. After the pre-treatment, the sample was cooled to 100 °C and saturated with ammonia. The temperature was increased from 100 to 600 °C at a constant heating rate of 10 °C/min under a He flow of 40 ml/min. The concentration of ammonia in the exit gas was monitored continuously with a TCD detector.

2.2. Methanol conversion

Methanol conversion was performed in a fixed-bed quartz tubular reactor at atmospheric pressure. In the pulse reactions, a catalyst

Table 1
Methanol conversion and product selectivity of MTO over ZSM-22.

| Pulse number | Conversion (%) | Selectivity (C%) | | | | | | | | |
|--------------|----------------|--------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|----------------|----------------|-----------------------------|
| | | CH ₃ OH | C ₁ ⁰ | C ₂ ⁰ | C ₂ ⁺ | C ₃ ⁰ | C ₃ ⁺ | C ₄ | C ₅ | C ₆ ⁺ |
| 1 | 76.5 | 2.3 | 3.7 | 0.4 | 22.3 | 3.4 | 17.2 | 28.6 | 22.1 | |
| 2 | 66.8 | 1.8 | 3.0 | 0.3 | 20.2 | 3.9 | 16.9 | 28.4 | 25.5 | |
| 5 | 63.7 | 2.1 | 3.0 | 0.3 | 19.6 | 3.4 | 16.3 | 28.7 | 26.6 | |
| 15 | 53.7 | 2.5 | 3.0 | 0.3 | 19.3 | 3.2 | 15.8 | 27.8 | 28.1 | |
| 19 | 40.4 | 3.3 | 3.0 | 0.2 | 20.0 | 2.7 | 15.7 | 27.8 | 27.3 | |

sample of 45 mg (60–80 mesh) was loaded into the reactor and activated at reaction temperature (450 °C) for 1 h before reaction. The reactions were carried out at 450 °C with reactant-catalyst contact time of 0.08 s. An injection of methanol of 1 µl was conducted onto the catalyst, and the effluent was kept warm and analyzed by online gas chromatography (Varian GC3800) equipped with a PoraPLOT Q-HT capillary column and a FID detector. For the ¹³C labeling experiments, pre-reaction of 15 pulses of ¹²C-methanol injections was followed by successive ¹³C-methanol injections. The effluent products of each ¹³C-methanol pulse reaction were collected and analyzed by an Agilent 6890/5973N MSD GC-MS.

In the continuous flow reactions, a catalyst sample of 120 mg was loaded into the reactor and activated at the reaction temperature (450 °C) for 1 h. The methanol was fed by passing the carrier gas (8.5 ml/min) through a saturator containing methanol at 24 °C, which gave a WHSV of 1.0 h⁻¹. The effluent was analyzed by online gas chromatography. After the reaction, the discharged catalyst was extracted and determined by GC-MS, following the method introduced by Guisnet [23].

2.3. Computational modeling

Computational modeling and geometry optimization of the selected materials within the zeolite channels were performed using FORCITE program in MATERIAL STUDIO. For simplicity, the ZSM-22 was modeled as pure silica TON type zeolite. The unit cell and atomic coordinates for the framework was taken from the known crystal structure of the TON structure [24]. The zeolite lattice was held fixed during the simulation and the organic species was allowed to move freely in the channels. All of the calculations were performed using Universal Forcefield.

3. Results and discussion

3.1. Pulse reaction of methanol using ¹³C labeling

Methanol conversion over ZSM-22 was performed on the pulse reaction system using ¹³C labeling technique and the results are displayed in Table 1 and Figs. 1 and 2. The conversion in the context was referred to the percent of methanol which were converted into hydrocarbons, that is to say, dimethylether was also considered as reactant in the following discussion.

The methanol conversion was 76.5% for the first methanol injection and decreased in the following injections. After 19 injections of methanol were conducted, methanol conversion was 40.4%. Propene was one of the main products with a selectivity of ~20%, while very low ethene selectivity (only 3%) was observed. The selectivities for C₅ and C₆⁺ were in the range of 22–29% and most of the C₆⁺ were olefins. It was noticeable that the deactivation appeared over ZSM-22 since the second methanol injection. This means that no induction period was observed over ZSM-22.

In the ¹³C labeling experiments, after 15 times of ¹²C-methanol pulse reactions were performed, 4 pulses of the ¹³C labeling methanol were injected into reactor successively, and the isotopic

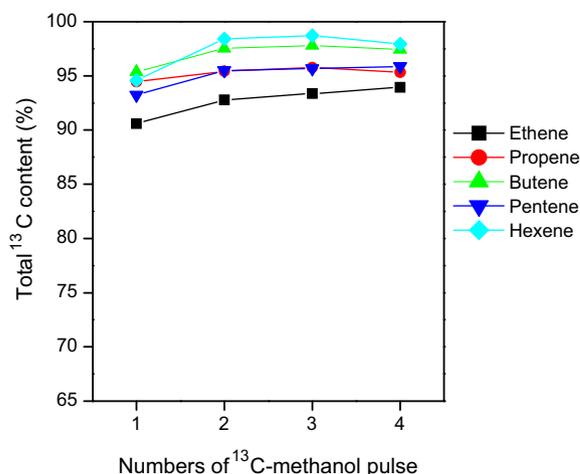


Fig. 2. Total ¹³C content in the effluent products of successive ¹³C-methanol pulse reaction over ZSM-22 at 450 °C after the pre-reaction of 15 pulses of ¹²C-methanol, CT=0.08 s.

distribution in the effluent of each pulse was analyzed by GC-MS and displayed in Fig. 1.

Isotopic distribution indicated that the product molecules containing only ¹³C atoms was predominant (>80%) in the effluent and the proportion of ¹³C-atoms into the products increased with the following ¹³C-methanol injection.

Different from the publications [19,20], in which the reactions were carried out under the continuous-flow conditions, the isotopic switch experiments in this study were performed on a pulse reaction system. In this setup, the mixing of ¹²C-methanol and ¹³C-methanol was avoided and the switch of ¹²C/¹³C could be clear-cut and an immediate products analysis after isotopic switch could be realized. This also makes it possible to correlate the differences in the ¹³C distribution to the reaction mechanism. ¹²C-methanol pre-reaction possibly generated ¹²C-coke species, such as polymethylbenzenes, in the cages or channels of the catalysts. The incorporation of ¹²C atom into the products would predict that the reaction followed hydrocarbon pool mechanism [4,5] and these ¹²C-coke species may work as the reaction centers of methanol conversion. Through another reaction route proposed for methanol conversion, olefin methylation-cracking [19,20,25–27] without involving the ¹²C-polymethylbenzenes retained in the catalysts, the products generation would be independent of the scrambling of isotopic distribution. However, if both of the two reaction mechanisms were allowed to operate on a specific catalyst, the products from the former reaction route would possibly serve as the initial olefins for the later reaction route, which makes the reaction route determination

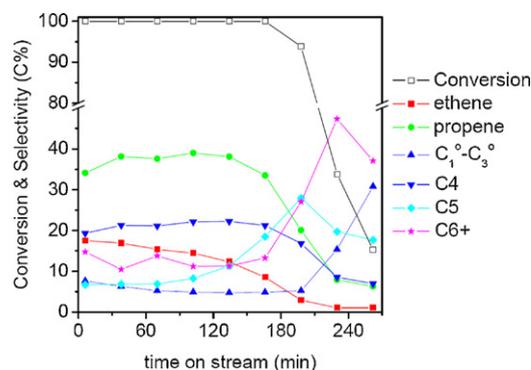


Fig. 3. Conversion of methanol and product selectivities of MTO reaction over HZSM-22 in fixed-bed reactor at 450 °C, WHSV = 1.0 h⁻¹, He/MeOH (mol) = 5.4.

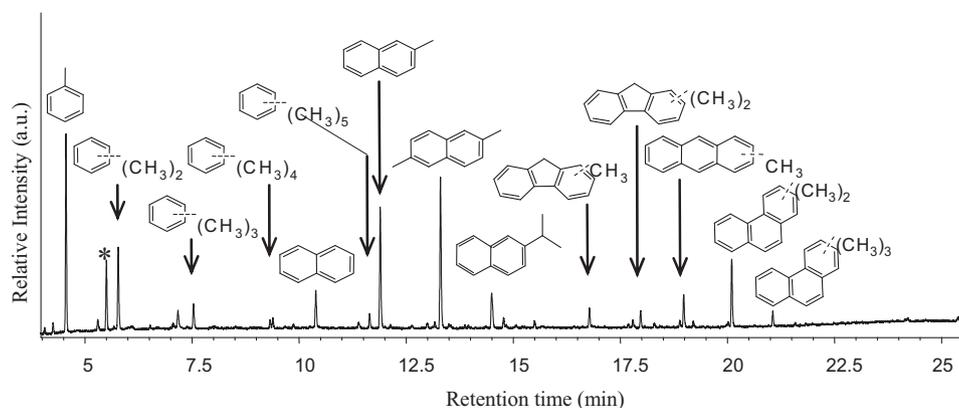


Fig. 4. GC-MS chromatogram of the compounds retained in the deactivated H-ZSM-22 catalyst of MTO conversion in the fixed bed reactor, * internal standard.

more difficult from the isotopic distribution. Anyway, the observations mentioned above in the ^{13}C switch experiments is still helpful for distinguishing the reaction route of methanol conversion over ZSM-22, even the conclusion is difficult to be drawn exactly.

The total ^{13}C contents of the products were calculated from the detailed isotopic distribution and plotted in Fig. 2 against the pulse number of ^{13}C methanol. The incorporation of ^{12}C atoms into the products over ZSM-22 was less obvious than that over SAPO-34 [28] and ZSM-5 [19,20], but ethene shows appreciable incorporation of ^{12}C atoms. At the 2nd to 4th pulse of ^{13}C methanol, the total ^{13}C contents of propene, butene, pentene and hexene were higher than 95%. As shown in Table 1, C_3^+ olefins were the main products of methanol conversion over ZSM-22. So it was reasonable to propose that methanol conversion over ZSM-22 mainly follows the olefin methylation-cracking mechanism. The incorporation of ^{12}C atoms into ethene over ZSM-22 was higher than that into C_3^+ olefins. This suggested that the ethene formation over ZSM-22 might be relevant with the hydrocarbon pool mechanism, as its formation over ZSM-5 [19]. However, lower selectivity for ethene was observed over ZSM-22 than that over ZSM-5.

The differences in the product distribution over ZSM-22 and ZSM-5 can be explained by taking the zeolite topology into account. ZSM-22 has only one dimensional 10 member ring channels with no intersections, so the largest space which ZSM-22 can offer was $5.7 \times 4.6 \text{ \AA}^2$. ZSM-5 also has the 10 member ring channels but it contains channel intersections which can accommodate cyclic species as hydrocarbon pool. Actually, large amount of toluene and xylene were detected among C_6^+ products over ZSM-5 [1]. Comparably, olefins accounted for the largest part of C_6^+ over ZSM-22. Considering the channel of ZSM-22 was too narrow for the reaction following the mechanism of hydrocarbon pool, the methanol conversion more possibly went through the olefin methylation and cracking route. This could explain the generation of large amount of high olefins ($>\text{C}_3^+$) and small amount of ethene over ZSM-22.

3.2. Continuous-flow reaction of methanol over ZSM-22

As shown in Table 1, in the pulse reactions deactivation of methanol conversion over ZSM-22 occurred very quickly. As mentioned above, the olefin methylation-cracking mechanism was the main reaction route for methanol conversion over ZSM-22, so the deactivation may stem from the quick diffusion of the olefins out of the catalyst channels, which makes the reaction cycle discontinued. At the same time, the deactivation from the blockage of the channels by coke species could still not be excluded. To shed light on this

issue, methanol conversion over ZSM-22 was also carried out in a fixed bed reactor at 450°C with the methanol WHSV of 1.0 h^{-1} . The conversion and product selectivity were plotted against the reaction time on stream in Fig. 3. Methanol conversion was 100% before 160 min of time on stream under present reaction conditions. These results further confirmed that under the continuous-flow condition with an appreciable contact time, the high reactivity over ZSM-22 could be kept for a long period, and suggest that the deactivation over ZSM-22 in pulse reactions might be associated with the quick diffusion of olefins from the catalyst channels and/or the depression of the olefins cracking by active sites coverage caused by the gradually deposited coke species.

In the continuous-flow conversion of methanol, before the catalyst became deactivated, propene was the main product and its selectivity increased from 35% to about 40%. At the same time, the ethene selectivity was in the range of 17–10%. During this period, the selectivities for ethene and propene were higher than that obtained in the pulse reaction. While the selectivities to C_5 and C_6^+ were lower than that obtained in the pulse reaction. This result suggests that the higher olefins might be cracked into lighter olefins under the condition of lower space velocity and longer reaction contact time in the continuous-flow fixed bed reactor.

It was noticeable that when the methanol conversion decreased to lower than 100% with prolonging the reaction time, the selectivities of ethene, propene and C_4 decreased rapidly, meanwhile the C_5 and C_6^+ selectivities increased. After ~ 190 min on stream, methanol conversion decreased sharply from 95% to $\sim 10\%$ and C_1^0 – C_3^0 alkanes selectivity increased. During this period, the selectivities of C_5 and C_6^+ increased to a maximum and then decreased (they were still higher than the selectivity for ethene, propene and C_4).

ZSM-22 was a TON type zeolite with only 1-dimensional channels and the channel openings of ZSM-22 were easy to be blocked by the coke species. The increase of alkanes selectivity after 190 min on stream indicates that the hydride transfer reaction became the main reaction, which led to heavier coking of the catalyst. This made the diffusion of the products out of the channels more difficult and further reaction more possibly occur. With coke deposition, the stronger acidic sites were easier to be covered by the coke and as a result the cracking of higher olefins was suppressed. These were responsible for the increase in heavier olefin production and the low efficiency in methanol conversion and the production of lighter olefin. The catalyst was completely deactivated when most of the channels of ZSM-22 catalyst were blocked. The materials retained in the discharged catalyst after reaction were analyzed by GC-MS and the chromatogram in Fig. 4 shows the retained organics were dominated by a large amount of aromatics, including polymethylbenzenes, naphthalenes, and phenanthrenes

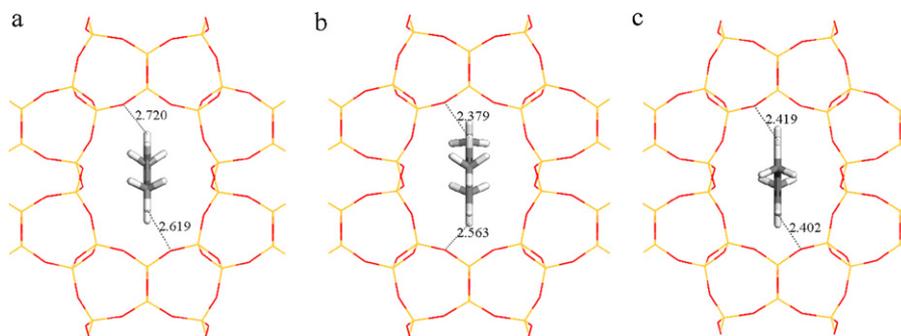


Fig. 5. Equilibrium geometry of *p*-xylene (a), 1,2,4-trimethylbenzene (b) and 2,6-dimethylnaphthalene (c) adsorbed in the channels of TON type pure silica zeolite.

Table 2

Adsorption energy of *p*-xylene, 1,2,4-trimethylbenzene and 2,6-dimethylnaphthalene in the channels of TON type pure silica zeolite.

| Adsorbed molecule | PX | TMB | DMN |
|------------------------------|-------|-------|-------|
| Adsorption energy (kcal/mol) | −42.9 | −43.0 | −54.4 |

(or anthracenes). These compounds with big size were possibly responsible for the deactivation of methanol conversion over ZSM-22.

The location of these coke species in the catalyst was still unknown. Some researchers [20,29,30] argued that ZSM-5 (MFI type with 10 member ring and intersections) cannot provide enough spaces for the formation of coke species larger than tetramethylbenzenes, and this was believed to be the reason of the long life time of ZSM-5 for methanol conversion. The deactivation of ZSM-5 was caused by the coke on the external surface of the zeolite crystals [29]. The diameter of ZSM-22 channels was close to that of ZSM-5, so the formation of the large coke species in the channels might also be suppressed. But the large species was detected in the coke analysis by GC–MS. They may form on the external surface or near the pore mouth. These species could age to insoluble graphitic species or be adsorbed in the channels (or near the pore mouth) and then blocked the pore openings. The adsorption of these species in the channels was confirmed by computational modeling of the selected materials within the pure silica TON type zeolite (the topology which ZSM-22 belongs to, for detailed structure information see [24]) using FORCITE program in MATERIAL STUDIO. Fig. 5 shows the energy minimized adsorption complexes of *p*-xylene (PX), 1,2,4-trimethylbenzene (TMB) and 2,6-dimethylnaphthalene (DMN) within the TON channels, and the adsorption energy is shown in Table 2. It can be seen that the adsorption energy was in the order of $PX \approx TMB < DMN$. This indicates that the DMN molecule size was more comparable with the TON channel than PX and TMB. The nearest distances of the adsorbed molecules to the zeolite wall were also displayed in Fig. 5. These results show that these large coke species could be adsorbed in the TON channels, but the void spaces might be too small for further reactions.

4. Conclusions

In summary, under the pulse reaction conditions, the methanol conversion over H-ZSM-22 showed high selectivity for olefins heavier than propene. Aided by ^{13}C labeling technique, it was revealed that the conversion mainly followed the olefin methylation-cracking reaction cycle, which was different from the report by Cui et al. [18]. The results obtained under the continuous-flow reaction conditions confirmed the feasibility of H-ZSM-22 for methanol-

to-olefins conversion. Furthermore, the GC–MS analysis of the retained coke species and computational modeling of them in ZSM-22 channels suggested that these coke species (such as polymethylated benzenes and naphthalenes) were responsible for the deactivation of ZSM-22 by blocking the zeolite channel openings, rather than acting as the active centers for olefins production.

Acknowledgments

The authors thank the Natural Science Foundation of China (Nos. 20903091 and 20973164) for financial support. The authors thank Prof. Tao Zhang for his valuable help in theoretical calculation.

References

- [1] M. Stocker, *Micropor. Mesopor. Mater.* 29 (1999) 3–48.
- [2] F.J. Keil, *Micropor. Mesopor. Mater.* 29 (1999) 49–66.
- [3] Z.M. Liu, C.L. Sun, G.W. Wang, Q.X. Wang, G.Y. Cai, *Fuel Process. Technol.* 62 (2000) 161–172.
- [4] U. Olsbye, M. Bjorgen, S. Svelle, K.P. Lillerud, S. Kolboe, *Catal. Today* 106 (2005) 108–111.
- [5] J.F. Haw, W.G. Song, D.M. Marcus, J.B. Nicholas, *Acc. Chem. Res.* 36 (2003) 317–326.
- [6] W. Wang, M. Hunger, *Acc. Chem. Res.* 41 (2008) 895–904.
- [7] D. Lesthaeghe, V. Van Speybroeck, G.B. Marin, M. Waroquier, *Ind. Eng. Chem. Res.* 46 (2007) 8832–8838.
- [8] I.M. Dahl, S. Kolboe, *J. Catal.* 149 (1994) 458–464.
- [9] I.M. Dahl, S. Kolboe, *Catal. Lett.* 20 (1993) 329–336.
- [10] I.M. Dahl, S. Kolboe, *J. Catal.* 161 (1996) 304–309.
- [11] W.G. Song, J.F. Haw, J.B. Nicholas, C.S. Heneghan, *J. Am. Chem. Soc.* 122 (2000) 10726–10727.
- [12] B. Arstad, S. Kolboe, *J. Am. Chem. Soc.* 123 (2001) 8137–8138.
- [13] B. Arstad, S. Kolboe, *Catal. Lett.* 71 (2001) 209–212.
- [14] P.W. Goguen, T. Xu, D.H. Barich, T.W. Skloss, W.G. Song, Z.K. Wang, J.B. Nicholas, J.F. Haw, *J. Am. Chem. Soc.* 120 (1998) 2650–2651.
- [15] D.M. McCann, D. Lesthaeghe, P.W. Kletnieks, D.R. Guenther, M.J. Hayman, V. Van Speybroeck, M. Waroquier, J.F. Haw, *Angew. Chem. Int. Ed.* 47 (2008) 5179–5182.
- [16] M. Seiler, W. Wang, A. Buchholz, M. Hunger, *Catal. Lett.* 88 (2003) 187–191.
- [17] W. Wang, Y.J. Jiang, M. Hunger, *Catal. Today* 113 (2006) 102–114.
- [18] Z.M. Cui, Q. Liu, W.G. Song, L.J. Wan, *Angew. Chem. Int. Ed.* 45 (2006) 6512–6515.
- [19] S. Svelle, F. Joensen, J. Nerlov, U. Olsbye, K.P. Lillerud, S. Kolboe, M. Bjorgen, *J. Am. Chem. Soc.* 128 (2006) 14770–14771.
- [20] M. Bjorgen, S. Svelle, F. Joensen, J. Nerlov, S. Kolboe, F. Bonino, L. Palumbo, S. Bordiga, U. Olsbye, *J. Catal.* 249 (2007) 195–207.
- [21] J.Z. Li, Y. Qi, Z.M. Liu, G.Y. Liu, D.Z. Zhang, *Catal. Lett.* 121 (2008) 303–310.
- [22] S. Teketel, S. Svelle, K.-P. Lillerud, U. Olsbye, *ChemCatChem* 1 (2009) 78–81.
- [23] M. Guisnet, L. Costa, F.R. Ribeiro, *J. Mol. Catal. A: Chem.* 305 (2009) 69–83.
- [24] <http://www.iza-structure.org/databases/>.
- [25] S. Svelle, P.A. Ronning, S. Kolboe, *J. Catal.* 224 (2004) 115–123.
- [26] S. Svelle, P.O. Ronning, U. Olsbye, S. Kolboe, *J. Catal.* 234 (2005) 385–400.
- [27] Z.M. Cui, Q. Liu, Z. Ma, S.W. Bian, W.G. Song, *J. Catal.* 258 (2008) 83–86.
- [28] B.P.C. Hereijgers, F. Bleken, M.H. Nielsen, S. Svelle, K.-P. Lillerud, M. Bjorgen, B.M. Weckhuysen, U. Olsbye, *J. Catal.* 264 (2009) 77–87.
- [29] T. Behrsing, H. Jaeger, J.V. Sanders, *Appl. Catal.* 54 (1989) 289–302.
- [30] L. Palumbo, F. Bonino, P. Beato, M. Bjorgen, A. Zecchina, S. Bordiga, *J. Phys. Chem. C* 112 (2008) 9710–9716.