

Efficient approach to the synthesis of *i*-propylbenzonitriles by selective ammoxidation

Guangyong Xie^{*1,2,3}, Aiqing Zhang²

¹Key Laboratory of Rubber-Plastics of Ministry of Education/Shandong Provincial Key Laboratory of Rubber -Plastics, Qingdao University of Science & Technology, Qingdao 266042, China

²Key Laboratory of Catalysis and Materials Science of Hubei Province, College of Chemistry and Materials Science, South-Central University for Nationalities, Wuhan 430074, China.

³Ministry of Education Key Laboratory for the Green Preparation and Application of Functional Materials, Hubei University, Wuhan 430062, China

Received: October 26, 2011; Revised: January 31, 2012

Abstract *i*-Propylbenzonitriles were prepared for the first time by direct selective ammoxidation of *i*-propylbenzyl chlorides obtained by chloromethylation of *i*-propylbenzene with high yields and nearly 100% selectivity at a relatively low temperature of *ca.* 200 °C.

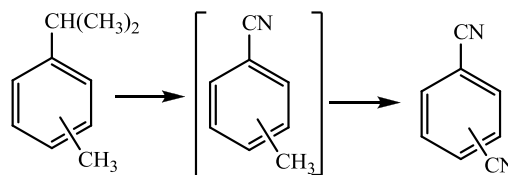
Key words: ammoxidation · *i*-propylbenzonitrile · *i*-propylbenzene · cymene · chloromethylation

INTRODUCTION

Aromatic nitriles are important industrial chemicals and valuable synthetic intermediates [1–5]. As one type of important aromatic nitriles, *i*-propylbenzonitriles can easily be converted to corresponding amides, acids, esters, amines, etc., which are commercially interesting and valuable intermediates for the synthesis of pharmaceuticals, pesticides, dyestuffs, fluorescence whiteners, and so on.

The basic assumption for all molecule based hypotheses is that similar molecules have similar activities. This principle is also called structure-activity relationship (SAR). Quantitative structure-activity relationship, QSAR, is the process by which chemical structure is quantitatively correlated with a well defined process, such as biological activity or chemical reactivity. Similar to other aromatic nitriles, *i*-propylbenzonitriles can generally be synthesized by dehydration of amides [6], cyanation of aromatic bromides [7], diazotization of propylaniline [8], etc. These methods usually need expensive materials or lead to serious pollution and are not suitable for industrial production on a large scale. In general, the heterogeneous catalytic ammoxidation of methyl aromatics is the most simple and economically most profitable route for the production of aromatic nitriles [1–5]. However, *i*-propylbenzonitriles cannot be synthesized by direct catalytic ammoxidation of cymenes, which would mainly produce dinitriles with a little tolunitriles,

due to the lower dissociation energy of the hydrogen at the α -C and the higher catalytic activity of the isopropyl group compared to the methyl group under gas phase ammoxidation conditions, as shown in Scheme 1.

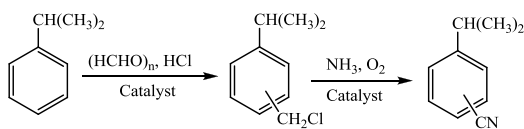


Scheme 1. Direct ammoxidation of cymenes

We have synthesized tolunitriles by selective ammoxidation of methylbenzyl chlorides prepared by chlorination of xylenes [9]. However, this reaction needs poisonous chlorine. Moreover, it is very difficult to controllably produce only alkylbenzyl chlorides by direct chlorination of methylaromatics, often along with the multi-chlorinated by-products. Here we report an efficient approach to the synthesis of *i*-propylbenzonitriles by selective ammoxidation of *i*-propylbenzyl chlorides prepared by chloromethylation of *i*-propylbenzene, as shown in Scheme 2. To the best of our knowledge, this is the first case to synthesize *i*-propylbenzonitriles by catalytic gas phase ammoxidation. Furthermore, this approach provides a new synthetic path to obtain alkylbenzonitriles and other aromatic nitriles, especially those having heat-sensitive

* To whom all correspondence should be sent:
E-mail: xxgy@hotmail.com

groups and not being prepared by direct ammoxidation.



Scheme 2. Synthesis of *i*-propylbenzonitriles by selective ammoxidation

EXPERIMENTAL

General

The reagents for the preparation of catalysts and *i*-propylbenzene were analytically or chemically pure. The VCrO/SiO₂ catalysts were prepared according to our previous works [10, 11]. The products were characterized by ¹H NMR, IR spectroscopy and elemental analysis. The ¹H NMR spectra were recorded on a Bruker AM-300 MHz spectrometer with tetramethylsilane as an internal standard. The IR spectra were measured on a Nicolet Nexus470 FT-IR spectrometer. Elemental analyses were carried out using Vario EL 111. The purity of the products was determined on a Shimadzu GC-17A gas chromatograph.

CHLOROMETHYLATION OF *I*-PROPYLBENZENE

The procedure for chloromethylation of *i*-propylbenzene was referred to our previous work [12]. The mixture of *i*-propylbenzyl chlorides was obtained by vacuum distillation in 93 % yields, b.p. 118 – 120°C / 35 mmHg.

SELECTIVE AMMOXIDATION OF *I*-PROPYLBENZYL CHLORIDES

The selective ammoxidation of *i*-propylbenzyl chlorides was carried out in a 30 mm-inside-diameter quartz tube fixed-bed reactor [10, 11, 13] loaded with 10 g catalyst. The *i*-propylbenzyl chlorides were fed by a micropump, vaporized and mixed in a preheated vessel with ammonia and air after having passed gas flowmeters with suitable molar ratios. The preheated gas flow was then fed directly into the reactor. The temperature was maintained at 220 ± 2°C. *i*-Propylbenzyl chlorides (PBCs) were introduced at a rate of 0.6 mL h⁻¹ and the molar ratios of air / PBCs and NH₃ / PBCs were 15 and 3, respectively. After the reaction, the outlet stream was cooled and the products were condensed in a condensing apparatus in 96 % yields. Pure *ortho*-*i*-propylbenzonitrile and *para*-*i*-propylbenzonitrile could be obtained by fractional distillation with 21 % (b.p. 72 – 75 °C / 5 mmHg)

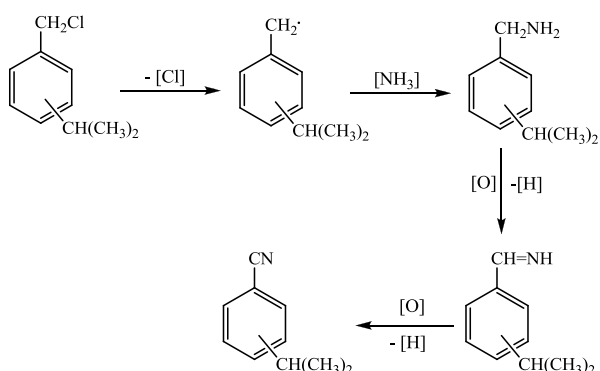
and 75 % (b.p. 88 – 90 °C / 5 mmHg) yields, respectively, and the purities were 98 % and 99 % by GC. Characterization data for *ortho*-*i*-propylbenzonitrile: ¹H NMR (300 MHz, CDCl₃): δ 7.45–7.63(m, 4H, Ph-*H*), 2.87(m, 1H, -CH(CH₃)₂), 1.23(d, 6H, -CH(CH₃)₂). IR(KBr, cm⁻¹): 2226 (-CN). Calcd for C₁₀H₁₁N: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.36; H, 7.85; N, 9.79. Characterization data for *para*-*i*-propylbenzonitrile: ¹H NMR (300 MHz, CDCl₃): δ 7.46–7.58 (m, 4H, Ph-*H*), 2.85(m, 1H, -CH(CH₃)₂), 1.20(d, 6H, -CH(CH₃)₂). IR(KBr, cm⁻¹): 2224 (-CN). Calcd for C₁₀H₁₁N: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.98; H, 7.71; N, 9.31.

RESULTS AND DISCUSSION

In ammoxidation of methylaromatics, the hydrogen extraction from the methyl group to generate the benzyl species is generally considered to be the rate-determining step of the reaction. Similar to the methyl group, the alkyl groups can also be converted to cyano groups under gas-phase ammoxidation conditions (*ca.* 400 °C), so alkylaromatics can also be ammoxidized to aromatic nitriles. Because the dissociation energies of the α-C-H bonds in different alkyl groups are different, the different alkyl groups existing on one benzene ring would have different reactivities. In the ammoxidation of cymene, the methyl and isopropyl groups are generally ammoxidized to cyano groups, but due to the lower dissociation energy of the hydrogen at α-C of the isopropyl group (350 kJ/mol) compared with the methyl group (370 kJ/mol) [14], the isopropyl group is more active and would thus more easily be ammoxidized to the cyano group. So, besides dinitriles, considerable amounts of tolunitriles would exist in the products [15]. *i*-Propylbenzonitriles cannot be prepared by direct ammoxidation of cymenes. We have previously prepared tolunitriles by selective ammoxidation of methylbenzyl chlorides [9]. Considering the lower C-Cl bond energy (290 kJ/mol) and the higher reactivity of the chloromethyl group, here we report a new route to prepare *i*-propylbenzonitriles from the inexpensive *i*-propylbenzene by chloromethylation to *i*-propylbenzyl chlorides, which could then be selectively ammoxidized to *i*-propylbenzonitriles at a relatively low temperature of *ca.* 200 °C (Scheme 2). The ammoxidation temperature of *i*-propylbenzyl chlorides is reduced by more than 100 °C compared with that of ordinary methylaromatics. At such a low temperature, the *i*-propyl group could not be

ammoxidized, so the selectivity for *i*-propylbenzonnitriles is very high, and the total molar yields of *i*-propylbenzonnitriles can reach 89 % calculated with respect to *i*-propylbenzene. The possible catalytic mechanism for ammoxidation of *i*-propylbenzyl chlorides is shown in Scheme 3.

Chloromethylation of *i*-propylbenzene can give *ortho*-*i*-propylbenzyl chloride and *para*-*i*-propylbenzyl chloride [12]. Because of the very close boiling points and similar reactivities under the ammoxidation conditions, *i*-propylbenzyl chlorides could not be separated but reacted as a mixture to afford the *i*-propylbenzonnitrile isomers, which can be separated by fractional distillation.



Scheme 3. Possible mechanism for ammoxidation of *i*-propylbenzyl chlorides.

The vanadium-containing mixed oxides are generally the most active and selective catalysts used for ammoxidation of methylaromatics. We have found that silica supported vanadium-chromium oxides [10, 11] show higher catalytic activity and selectivity at a lower reaction temperature than the corresponding unsupported vanadium-containing oxides for ammoxidation of methylaromatics. They could also be used for ammoxidation of *i*-propylbenzyl chlorides at very low temperature. The silica supported vanadium-chromium oxides were prepared according to our previous reports [10, 11]. With 10 wt.% of V-Cr loaded in the catalysts, highest catalytic activity and selectivity for ammoxidation of methylaromatics were registered. The X-ray diffraction (XRD) data show that V-Cr oxides exist as an amorphous phase in the 10 wt.% loadings [10]. With a V/Cr molar ratio of 1, the VCrO/SiO₂ catalyst shows best catalytic performance with 96% of yield and 98% of selectivity.

CONCLUSIONS

i-Propylbenzonnitriles were synthesized by selective ammoxidation of *i*-propylbenzyl chlorides prepared by chloromethylation of *i*-propylbenzene at low temperature in high yields and nearly 100% selectivity. This approach provides a new path to obtain alkylbenzonnitriles and other aromatic nitriles, especially for those having heat-sensitive groups and not being prepared by direct ammoxidation.

Acknowledgments This work was financially supported by the National Natural Science Foundation of China (40830852, 21172269), the Open Fund of Ministry of Education Key Laboratory for the Green Preparation and Application of Functional Materials, the Open Fund of Key Laboratory of Rubber-Plastics of Ministry of Education /Shandong Provincial Key Laboratory of Rubber-plastics (KF2010001) and the Natural Sciences Foundation of South-Central University for Nationalities (YZZ10005).

REFERENCES

1. A. Martin, B. Lücke, *Catalysis Today*, 57, 61 (2000).
2. B. Lücke, K.V. Narayana, A. Martin, K. Jähnisch, *Adv. Synth. Catal.*, 346, 1407 (2004).
3. C. Hong, Y. Li, *Chinese J. Chem. Eng.*, 14, 670 (2006).
4. F. Chen, Y. Wang, X. Zhan, *Chinese J. Chem. Eng.*, 13, 615 (2005).
5. Q. Zheng, C. Huang, G. Xie, C. Xu, Y. Chen, *Synth Commun.*, 29, 2349 (1999).
6. C.S. Rao, M. Rambabu, P. S. Srinivasan, *Synth. Commun.*, 19, 1431 (1989).
7. S. Ushijima, K. Moriyama, H. Togo, *Tetrahedron*, 67, 958 (2011).
8. H. Gilman, A.H. Blatt, *Org. Synth.*, 2, 514 (1956).
9. G. Xie, Q. Zheng, C. Huang, Y. Chen, *Synth. Commun.*, 33, 1103 (2003).
10. G. Xie, Q. Zheng, C. Huang, Y. Chen, *Indian J. Chem. A.*, 41, 963 (2002).
11. G. Xie, C. Huang, *Fine Chemicals (in Chinese)*, 24, 790 (2007).
12. G. Xie, N. Liu, L. Lei, H. Ai, *Journal of South Central University for Nationalities (Nat. Sci. Edition)*, 28, 8 (2009).
13. G. Xie, C. Huang, *Indian J. Chem. Technol.*, 14, 371 (2007).
14. Y. Luo, *The Data Handbook of Chemical Bond Energies*, Science Press, Beijing, 2005.
15. B.V. Suvorov, S.R. Rafikov, B. A. Zhubanov, *Zh. Prikl. Khim.*, 36, 1837 (1963).

ЕФЕКТИВЕН ПОДХОД ЗА СИНТЕЗИРАНЕ НА ИЗО-ПРОПИЛБЕНЗОНИТРИЛИ, ЧРЕЗ
СЕЛЕКТИВНО АМОКСИДИРАНЕ

Гуангйонг Ксие^{*,1,2,3}, Аикинг Чанг²

¹ Централна лаборатория по каучук и пластмаса към Министерството на образованието/ Централна лаборатория в провинция Шандонг по каучук и пластмаса, Университет по наука и технология Кингдао, Кингдао 266042, Китай

² Централна лаборатория по катализ и материалознание в провинция Хубей, Колеж по химия и материалознание, Южноцентрален Университет за националностите, Ухан 430074, Китай

³ Централна лаборатория за зелено производство и приложение на функционални материали на Министерството на образованието, Университет Хубей, Ухан 430062, Китай

Постъпила на 26 октомври, 2011, преработена на 31 януари 2012

(Резюме)

Синтезирани са за първи път изо-пропилбензонитрили чрез директно селективно амоксидиране от i-пропилбензилни хлориди, получени чрез хлорметиране на i-пропилбензен с висок добив и почти 100% селективност при сравнително ниска температура от около 200°C.