World Academy of Science, Engineering and Technology
International Journal of Chemical and Molecular Engineering
Vol:7, No:7, 2013

Nano-Alumina Sulfuric Acid: An Efficient Catalyst for the Synthesis of α-Aminonitriles Derivatives

Abbas Teimouri, Alireza Najafi Chermahini, and Leila Ghorbanian

***Abstract*—**An efficient and green protocol for the synthesis of α-aminonitriles derivatives by one-pot reaction of different aldehydes with amines and trimethylsilyl cyanides has been developed using natural alumina, alumina sulfuric acid (ASA), nano-γ-alumina, nano-alumina sulfuric acid (nano-ASA) under microwave irradiation and solvent-free conditions. The advantages of methods are short reaction times, high yields, milder conditions and easy work up. The catalysts can be recovered for the subsequent reactions and reused without any appreciable loss of efficiency.

***Keywords*—**Nano-γ-alumina, nano-alumina sulfuric acid, green synthesis, microwave irradiation, α-aminonitriles derivatives.

I. Introduction

ALPHA-AMINONITRILES are significantly important intermediates for the synthesis of a wide variety of amino acids, amides, diamines, and nitrogen-containing heterocycles. [1] Among the methods reported for the synthesis of a-aminonitriles, nucleophilic addition of cyanide ion to imines (Strecker reaction), is of great importance to modern organic chemistry as it offers one of the most direct and viable methods for the synthesis of α-aminonitriles [2].

Thus, several modifications of the Strecker reaction have been developed using a variety of cyanide reagents such as alkaline cyanides, [3] Et_2AlCN, [4] $(EtO)_2$-$POCN_9$, [5], acetone cyanohydrins, [6] HCN, [7] KCN, [8] TMSCN, [9] Bu_3SnCN, [10] MeCOCN, [11], ethyl cyanoformate, [12], $Zn(CN)_2$ [13], $K_4[Fe(CN)_6]$, [14] along with catalysts variant such as $InCl_3$, [15] $BiCl_3$, [16], InI_3, [17], RhI_3 [18], $NiCl_2$, [19] $RuCl_3$, [20], [bmim]BF4 [21], montmorillonite KSF clay [22], silica sulfuric acid [23], silica-based scandium(III), [24] Silica-supported heteropoly acids [25], silica-bonded Sulfamic Acid [26] and Ga-TUD-1[27].

In continuation of our investigations on the use of novel synthetic methodologies in a heterogeneous system through multi-component procedures [28], here we present our recent studies on the synthesis of α-aminonitriles derivatives by one-pot reaction of different aldehydes with amines and trimethylsilyl cyanides in the presence of natural alumina, alumina sulfuric acid, nano-γ-alumina, nano-alumina sulfuric under microwave irradiation and solvent-free conditions.

A. Teimouri is with the Department of Chemistry, Payame Noor University (PNU), Isfahan, P.O. Box: 81395-671, Iran, (phone: 0098-311-3521804; fax: 098-311-3521802; e-mail: a_teimouri@pnu.ac.ir).

A. Najafi Chermahini was with the Department of Chemistry, Isfahan University of Technology, Isfahan, 841543111, Iran.

L. Ghorbanian was with the Materials Engineering Department, Isfahan University of Technology, Isfahan, Iran.

II. Experimental

A. Material

All reagents were purchased from Merck used without further purification. Products were characterized by spectroscopy data (IR, FTIR, ^{1}H NMR and ^{13}C NMR spectra), elemental analysis (CHN) and melting points. A JASCO FT/IR-680 PLUS spectrometer was used to record IR spectra using KBr pellets. NMR spectra were recorded on a Bruker 400 Ultrasheild NMR and DMSO-d6 was used as solvent. Melting points reported were determined by open capillary method using a Galen Kamp melting point apparatus and are uncorrected. Mass Spectra were recorded on a Shimadzu Gas Chromatograph Mass Spectrometer GCMS-QP5050A/Q P5000 apparatus. The reactions were performed using a microwave oven with a power of 600 W specially designed for organic synthesis.

B. Catalyst Preparation

1. Preparation of Alumina-Sulfuric Acid

The alumina-sulfuric acid was prepared by sol–gel method according to a procedure described [29]. A 500mL suction flask was used. It was equipped with a constant pressure dropping funnel containing freshly distilled chlorosulfonic acid (2.75ml, 41.2mmol) was charged with neutral alumina (10g, 100mmol) dried at 120°C for 2h with stirring. Chlorosulfonic acid was added drop wise over a period of 30 min at room temperature. The liberated HCl was removed through a $CaCl_2$ drying tube under reduced pressure to a water trap. Then it was kept in this condition for 1h at room temperature, was washed with distilled water several times, ethanol (2 times) and dried at 130°C for 4h.

2. Synthesis of Nano-γ-Al_2O_3 Catalyst

The nano-γ-Al_2O_3 was prepared by sol–gel method according to a procedure described [30]. In a typical experiment, Aluminum nitrate (15.614g) was added to 400ml of deionized water. Similarly solution of sodium carbonate is prepared by dissolving (7.95g) in 400ml of deionized water. 200ml of deionized water is taken in a 2 l capacity round-bottom flask and stirred well using magnetic stirrer. Then sodium carbonate and aluminum nitrate solutions are added to 200ml of deionized water (from separate burettes) drop wise.

The temperature was maintained 70°C during experiment. The pH after precipitation was found to be in the range of 7.5–8.5. The mixture was stirred for 4h. The digested precipitates were filtered and re-dispersed again in hot 2 l of deionized water, filtered and finally washed with ethanol first followed

by acetone to avoid contamination of 'Na' ions; and air dried at room temperature. The dried precipitates were calcined in a furnace at 550°C for 5h to produce nano-sized γ-Al_2O_3 powders.

3. Synthesis of nano-ASA

For synthesis of nano-ASA, In a 500ml round-bottom flask, chloro-sulfonic acid (1.35ml) was added drop wise to the high surface area nano-γ-Al_2O_3 (5g) over a period of 30min at room temperature. The components were mixed with constant stirring about 30min at ambient temperature to afford the nano-ASA as a uniform white solid. The liberated HCl was removed through a $CaCl_2$ drying tube under reduced pressure to a water trap. The solid phase obtained was washed with distilled water several times, dried at 130°C for 4 hours.

C. Characterization

X-ray diffraction pattern were recorded on diffractometer (Philips X'pert) using Cu Kα radiation (λ=1.5405Å), Crystallite size of the crystalline phase was determined from the peak of maximum intensity by using Scherrer formula, [31] with a shape factor (K) of 0.9, as below: Crystallite size = K.λ/W.cosθ, where, $W=W_b-W_s$ and W_b is the broadened profile width of experimental sample and W_s is the standard profile width of reference silicon sample. FT-IR spectra of the catalysts were recorded by FT-IR spectrophotometer in the range of 400–4000cm^{-1} with a resolution of 4cm^{-1} by mixing the sample with KBr.

Fig. 1 indicates the formation of crystallized alumina, as broad peaks indexed for γ-Al_2O_3 are seen in the XRD pattern, where small and broad peaks started appearing at 2θ =48° and at 2θ =67°. The broadening of the XRD peaks revealed the nano-size nature of γ-Al_2O_3 particles in alumina samples.

The morphology of the catalysts was studied. SEM micrographs have been presented in Fig. 2. The SEM picture showed that the particles were of irregular shape with a wide distribution of size. A part of the spectra data has been published in our previous work [28].

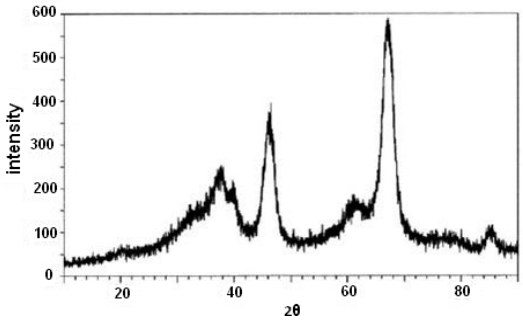

Fig. 1 XRD pattern of nano-γ-alumina catalyst

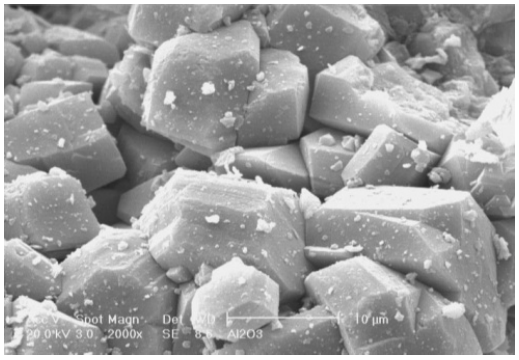

Fig. 2 SEM micrograph of nano-γ-alumina catalyst

D. General Procedure for the Synthesis of α-Aminonitriles Derivatives

To the reaction mixture of aldehyde (1mmol), amine (1 mmol), trimethylsilyl cyanide (1.5mmol) catalyst (10mg) was subjected to microwave irradiation (600W) at 90°C for 15 min. The reaction was monitored by TLC. After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and washed with EtOAc (2×20mL and the catalyst was separated by filtration. The organic solvent was removed under reduced pressure. After purification by chromatography on silica gel (ethyl acetate/n-hexane 20:80) α-aminonitriles were obtained.

- 2-(N-anilino)-2-phenyl acetonitrile (**1a**) Mp: 72-74°C; FTIR (KBr, cm^{-1}): 3334, 3023, 2946, 2234, 1603, 1517, 1280, 954, 750; ^{1}H NMR (400 MHz, DMSO-d6): δ 3.98 (bs, 1H), 5.42 (s, 1H), 6.74 (d, J = 7.6 Hz, 2H), 6.86 (t, J = 7.4 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 2H), 7.40 (m, 3H), 7.58 (m, 2H).; ^{13}C NMR (400 MHz, DMSO-d6): δ 49.88, 114.19, 118.14, 119.95, 127.29, 129.33, 129.61, 129.56, 133.99, 144.56; MS (m/z): 208.10 (M^+). Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45. Found: C, 80.56; H, 5.63; N, 13.32.
- 2-(4-Nitrophenyl)-2-(phenylamino) acetonitrile (**1b**) Mp: 90-92°C; FTIR (KBr, cm^{-1}): 3312, 3019, 2246, 1666, 1590, 1466, 1103, 756; ^{1}H NMR (400 MHz, DMSO-d6): δ 4.13 (d, J = 8.0 Hz, 1H), 5.20 (d, J = 8.0 Hz, 1H), 6.64 (d, J = 8.0 Hz, 2H), 6.75 (t, J = 7.8 Hz, 1H), 7.05 (t, J = 7.8 Hz, 2H), 7.52 (d, J = 8.05 Hz, 2H), 7.95 (d, J = 8.05 Hz, 2H); ^{13}C NMR (400 MHz, DMSO-d6): δ 49.31, 114.32, 115.74, 118.18, 119.46, 123.91, 127.84, 129.33, 144.89, 156.63; MS (m/z): 253.09 (M^+). Anal. Calcd for $C_{14}H_{11}N_3O_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.29; H, 4.22; N, 16.43.
- 2-(N-Anilino)-2-(4-hydroxyphenyl) acetonitrile (**1c**) Mp: 120-122 °C; FTIR (KBr, cm^{-1}): 3344, 3029, 2236, 1606, 1263, 1157, 834, 748; ^{1}H NMR (400 MHz, DMSO-d6): δ 4.53 (br s, 1H), 5.16 (s, 1H), 6.75–6.90 (m, 5H), 7.23 (t, J = 7.4 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 9.81 (br s, 1H); ^{13}C NMR (400 MHz, DMSO-d6): δ 49.36, 113.78, 115.65, 118.48, 119.29, 124.31, 128.46, 129.13, 145.39, 156.28; MS (m/z): 224.09 (M^+). Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 74.71; H, 5.21; N, 12.33.
- 2-(N-Anilino)-2-(4-methylphenyl) acetonitrile (**1d**) Mp: 70-72 °C; FTIR (KBr, cm^{-1}): 3311, 3025, 2236, 1665,

1559, 1254, 1121, 761; ^{1}H NMR (400 MHz, DMSO-d6): δ 2.36 (s, 3H), 3.52 (bs, 1H), 5.31 (s, 1H), 6.61 (d, *J* = 7.6 Hz, 2H), 6.75 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 4H), 7.64 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (400 MHz, DMSO-d6): δ 21.42, 50.13, 114.33, 117.93, 120.16, 127.09, 129.44, 129.90, 131.18, 139.42, 145.15; MS (m/z): 222.12 (M^+). Anal. Calcd for $C_{15}H_{14}N_2$: C, 81.08; H, 6.35; N, 12.59. Found: C, 65.20; H, 6.21; N, 12.43.

- 2-(N-anilino)-2-(4-methoxy-phenyl)-acetonitrile (**1e**) Mp: 94-96 °C; FTIR (KBr, cm^{-1}): 3432, 2920, 2234, 1596, 1512, 1245, 1176, 822, 746, 680; ^{1}H NMR (400 MHz, DMSO-d6): δ 3.82 (s, 3H), 3.94 (s, 1H), 5.32 (s, 1H), 6.74 (d, *J* = 8.7 Hz, 2H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 2H), 7.46 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (400 MHz, DMSO-d6): δ 49.78, 55.66, 114.14, 114.63, 118.40, 120.20, 126.12, 128.62, 129.58, 144.73, 160.43; MS (m/z): 238.11 (M^+). Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.45; H, 5.58; N, 11.70. Found: C, 75.34; H, 5.38; N, 11.56.
- 2-(N-anilino)-2-(4-chlorophenyl) acetonitrile (**1f**) Mp: 108-110 °C; FTIR (KBr, cm^{-1}): 3316, 3026, 2950, 2239, 1606, 1458, 1263, 1240, 887, 758; ^{1}H NMR (400 MHz, DMSO-d6): δ 4.04 (bs, 1H), 5.42 (s, 1H), 6.74 (d, 2H, *J* = 7.6 Hz), 6.91 (t, 1H, *J* = 7.4 Hz), 7.26 (t, 2H, *J* = 8.9 Hz), 7.48 (d, 2H, *J* = 8 Hz), 7.54 (d, 2H, *J* = 8 Hz); ^{13}C NMR (400 MHz, DMSO-d6): δ 164.73, 164.33, 142.26, 131.60, 129.76, 129.03, 126.88, 124.04, 121.16, 21.66; MS (m/z): 242.06 (M^+). Anal. Calcd for $C_{14}H_{11}ClN_2$: C, 69.28; H, 4.57; N, 11.54. Found: C, 69.11; H, 4.43; N, 11.32.
- 2-(4-Bromophenylamino)-2-phenylacetonitrile (**1g**) Mp: 100-102 °C; FTIR (KBr, cm^{-1}): 3325, 3038, 2963, 2235, 1599, 1228, 928, 762; ^{1}H NMR (400 MHz, DMSO-d6): δ 3.98 (sb, 1H), 5.32 (s, 1H), 6.64 (d, 2H, *J* = 8.3 Hz), 6.64 (t, 1H), 7.19 (t, 2H), 7.30 (d, 2H, *J* = 8.3 Hz), 7.52 (m, 2H); ^{13}C NMR (400 MHz, DMSO-d6): δ 49.94, 113.42, 116.71, 119.81, 124.46, 128.62, 129.66, 132.37, 133.44, 143.38; MS (m/z): 286.01 (M^+). Anal. Calcd for $C_{14}H_{11}BrN_2$: C, 58.56; H, 3.86; N, 9.76. Found: C, 58.44; H, 3.56; N, 9.63.

III. Results and Discussion

In an effort to develop an optimal catalytic system, various reaction parameters like effect of catalyst loading, and time for the preparation of α-aminonitriles derivatives were studied. The results listed in Table I showed that the conversions were sensitive to the catalyst type. The results showed that nano-alumina sulfuric acid promoted the reaction more effective than alumina sulfuric acid, nano-γ-alumina as far as the amount of catalyst and reaction times are concerned. One reason for increase the catalytic activity may be related to the number of available active sites. In order to evaluate the effect of the catalyst particle size on the catalytic activity, the results were compared with those obtained using alumina sulfuric acid (ASA). No good activity was observed in the presence of alumina sulfuric acid or natural alumina. In comparison with conventional methods, microwave irradiation reactions are cleaner and microwave irradiation decreased remarkably the reaction times. No side products were detected in these reactions. Microwave irradiation affords the respective products in only 5–10min. 10% of the expected product was obtained in the absence of catalyst. To further improve the yield and to optimize the reaction conditions, the same reaction was carried out in the presence of (10mg) of catalyst under similar conditions. Reaction with 10mg of the catalyst required a longer reaction time and the yield of product was dramatically increased up to 85% after irradiating the mixture for only 10min.

To minimize the formation of by-products and to achieve good yield of the desired product, the reaction is optimized by varying the amount of catalyst (15, 20 and 25mg). An increase in the amount of nano-ASA from 10 to 15mg increased the yield of the desired product to a great extent (85–96%). The percentage yield of the product with 10, 15, 20 and 25mg of alumina sulfuric acid as the catalyst are 85%, 96%, 84% and 76%, respectively. For the nano-γ-alumina and natural alumina as the catalyst, when the catalyst content was increased to 25mg, the product yield decreased to 65% and 54% respectively. Therefore, it was found that the use of 15 mg of the catalyst was sufficient to promote the reaction, and higher amounts of the catalyst did not increase the yields significantly. The temperature and the MW power were also optimized and the best results were obtained using 15mg of nano-ASA in 90^{o}C at 600 W.

No increase in yield was observed at higher temperatures, while lowering the temperature below 90^{0}C reduced the reaction rate.

On reaching the optimized conditions a wide range of α-aminonitriles were synthesized by using aromatic aldehydes with electron-donating or electron-withdrawing groups. Most of the aldehydes reacted efficiently with aniline and TMSCN to furnish the corresponding products in excellent yields (65-96%).

A proposed mechanism for the rule of various types of alumina catalysts in the reaction of aromatic aldehyde, amine and trimethylsilyl cyanide is presented in Fig. 1.

We propose a mechanism for the formation of α-aminonitriles derivatives 1(a–g) it has been hypothesized that the reaction proceeds. First, aromatic aldehyde activated by the acidic proton of alumina reacts with amines to form a key intermediate. Finally, nucleophilic addition of cyanide ion to the intermediate, which is formed from condensation of aldehydes and amines, yields α-aminonitriles derivatives.

TABLE I
Effect of Amount of Catalyst on the Synthesis of A-Aminonitriles Derivatives [A]

Entry	Catalyst	Catalyst loading (mg)	Time (min)	Yield (%)[b]
1		-	120	10
2	nano-ASA	10	10	85
3		15	5	96
4		20	5	84
5		25	5	76

[a] bezaldehyde (1 mmol), aniline (1 mmol) and trimethylsilyl cyanide (1.5 mmol)
[b] Yields after isolation of products

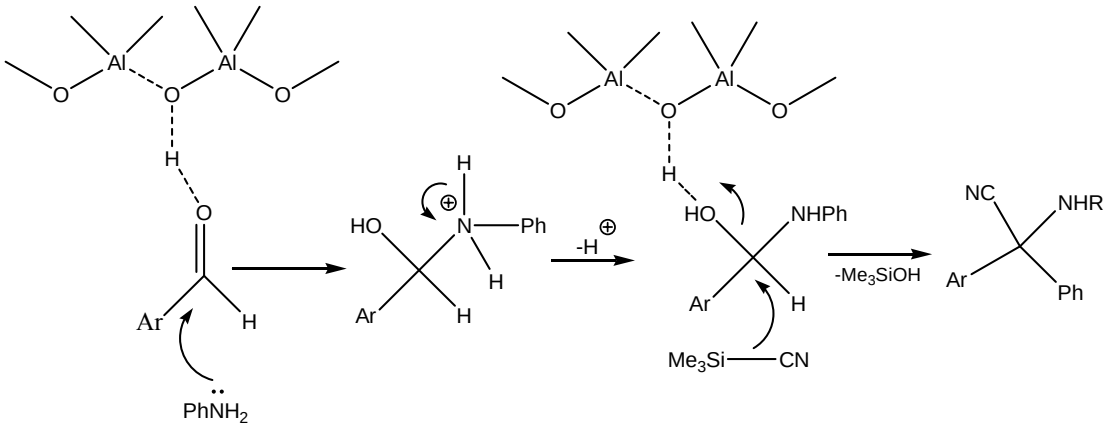

Fig. 3 Proposed mechanism for one-pot synthesis of α-aminonitriles derivatives

IV. Conclusions

In conclusion, we have demonstrated an efficient, versatile and convenient method for the synthesis of α-aminonitriles derivatives in reaction of different aromatic aldehyde with acyl hydrazide under microwave irradiation without solvent. A comparison of the catalytic efficiency of natural alumina, alumina sulfuric acid, nano-γ-alumina, nano-alumina sulfuric acid with the nano-alumina sulfuric acid exhibiting greater activity has also been demonstrated. Compared to previously reported methods, Moreover, the mild reaction conditions, high yields, easy work-up, clean reaction profiles and lower catalyst loading render this approach as an interesting alternative to the existing methods.

Acknowledgment

Supports from the Payame Noor University in Isfahan research council and helps of Isfahan University of Technology are gratefully acknowledged.

References

[1] R. O. Duthaler, Tetrahedron. 50 (1994) 1539-1650.
[2] H. Groger, Chem. Rev. 103 (2003) 2795-2827.
[3] S. Kobayashi, H. Ishitani, Chem. Rev. 99 (1999) 1069-1094.
[4] S. Nakamura, N. Sato, M. Sugimoto, T. Toru, Tetrahedron: Asymmetry 15 (2004) 1513-1516.
[5] S. Harusawa, Y. Hamada, T. Shioiri, Tetrahedron Lett. 20 (1979) 4663-4666.
[6] A. S. Paraskar, A. Sudalai, Tetrahedron Lett. 47 (2006) 5759-5762.
[7] D. Enders, J. P. Shilvock, Chem. Soc. Rev. 29 (2000) 359–373.
[8] S. Kobayashi, H. Ishitani, Chem. Rev. 99 (1999) 1069–1094.
[9] K. Shen, X. H. Liu, Y. F. Cai, L. L. Lin, X. M. Feng, Chem. Eur. J. 15 (2009) 6008–6014.
[10] Z. F. Xie, G. L. Li, G. Zhao, J. D. Wang, Synthesis (2009) 2035–2039.
[11] F. Cruz-Acosta, A. Santos-Exposito, P. Armas, F. Garcia-Tellado, Chem. Commun. 2009, 6839–6841.
[12] J. P. Abell, H. Yamamoto, J. Am. Chem. Soc. 131 (2009) 15118–15119.
[13] Sakshi Shah, Baldev Singh, Tetrahedron Letters 53 (2012) 151–156.
[14] Zheng Li, Yuanhong Ma, Jun Xu, Jinghong Shi, Hongfang Cai Tetrahedron Letters 51 (2010) 3922–3926.
[15] B. C. Ranu, S. S. Dey, S. Hajra, Tetrahedron 58 (2002) 2529–2532.
[16] S. K. De, R. A. Gibbs, Tetrahedron Lett. 45 (2004) 7407–7408.
[17] Z. L. Shen, S. J. Ji, T. P. Loh, Tetrahedron 64 (2008) 8159–8163.
[18] A. Majhi, Sung Soo Kim, S. T. Kadam, Tetrahedron 64 (2008) 5509–5514.
[19] S. K. De, J. Mol. Catal. A: Chem. 225 (2005) 169–171.
[20] M. North, Angew. Chem., Int. Ed. 43 (2004) 4126–4128.
[21] J.S. Yadav, B.V.S. Reddy, B. Eshwaraiah, New J. Chem. 27 (2003) 462-465.
[22] J.S. Yadav, B.V.S. Reddy, B. Eswaraiah, Tetrahedron 60 (2004) 1767-1771.
[23] W.Y. Chen, J. Lu, Synlett (2005) 2293-2296.
[24] B. Karimi, A. A. Safari, J. Organomet. Chem. 693 (2008) 2967–2970.
[25] Ezzat Rafiee, Solmaz Rashidzadeh, Alireza Azad, Journal of Molecular Catalysis A: Chemical 261 (2007) 49–52.
[26] T. Rahi, M. Baghernejad, K. Niknam, Chin. J. Catal., 33 (2012) 1095–1100.
[27] B. Karmakar, A. Sinhamahaparta, A. Baran Panda, J.Banerji, B. Chowdhury, Applied Catalysis A: General, 392 (2011) 111-117.
[28] A. Teimouri, A. Najafi Chermahini, J. Mol. Catal A: Chem. 346 (2011) 39-45.
[29] H. Shargi, M. H. Sarvari, R. Eskandari, J. Chem. Res. (2005) 483-486.
[30] K.M. Parida, Amaresh C. Pradhan, J. Das, Nruparaj Sahu Mat. Chem. Phys. 113 (2009) 244–248.
[31] B.D. Cullity, S.R. Stock, Elements Of X-Ray Diffraction, Third Edition Prentice Hall, Upper Saddle River, NJ, 2001 Pp. 388.