

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
مجری: اهرم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
www.Processconf.ir

Design new hybrid catalyst based SBA-15 as solid acid Nanoreactor for one-pot three-componentsynthesis of 2H-indazolo[2,1-b]phthalazine-triones

Habibollahghazizadeh,^{a,*} AlirezaSedrpoushan,^aHojatVeisi,^bMasoudHeidari^a

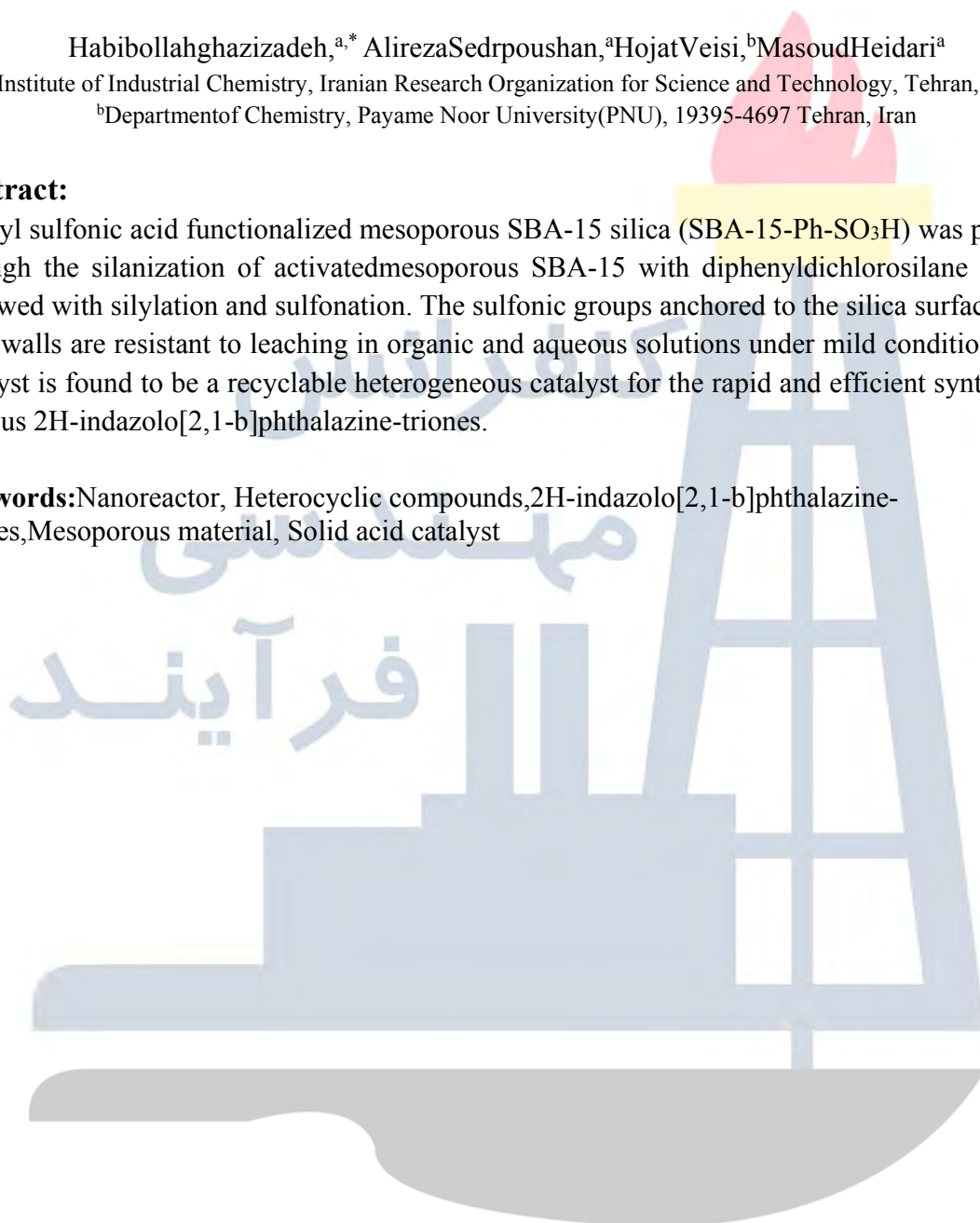
^aInstitute of Industrial Chemistry, Iranian Research Organization for Science and Technology, Tehran, Iran

^bDepartmentof Chemistry, Payame Noor University(PNU), 19395-4697 Tehran, Iran

Abstract:

Phenyl sulfonic acid functionalized mesoporous SBA-15 silica (SBA-15-Ph-SO₃H) was prepared through the silanization of activatedmesoporous SBA-15 with diphenyldichlorosilane (DPCS) followed with silylation and sulfonation. The sulfonic groups anchored to the silica surface of the pore walls are resistant to leaching in organic and aqueous solutions under mild conditions. This catalyst is found to be a recyclable heterogeneous catalyst for the rapid and efficient synthesis of various 2H-indazolo[2,1-b]phthalazine-triones.

Keywords:Nanoreactor, Heterocyclic compounds,2H-indazolo[2,1-b]phthalazine-triones,Mesoporous material, Solid acid catalyst



مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
مجری: احم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
www.Processconf.ir

Introduction:

In recent years, organically functionalized ordered Mesoporoussilicas [1-4] with a tunable pore structure, high surface areas and tailored composition has received great attention with broad application ranging from adsorbent [5-8], particularly SBA-15 between other silica materials, have relatively good hydrothermal stability, and possesses hexagonal arrays of uniform pores with high special surface area and large pore volume. The direct synthesis involving co-condensation of siloxane and organosiloxane species in the presence of different templating surfactants has been shown to be a promising alternative to the grafting procedures [9-12]. The covalent attachment of sulfonic acid groups to the surface of silica derivatives, several types of solid sulfonic acids, based on ordered mesoporoussilicas, have been created in recent years [13-23].

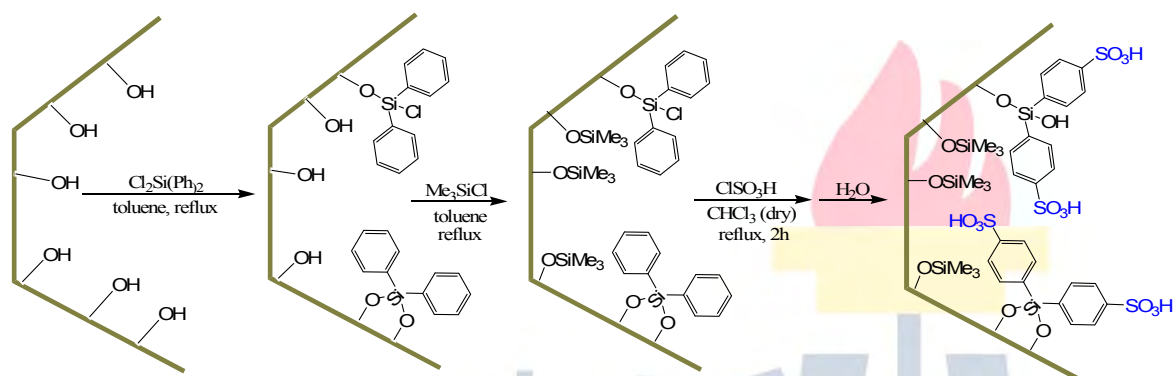
Multi-component reactions (MCRs) have proven to be a valuable asset in organic and medicinal chemistry [24-26]. Such protocols can be used for drug design, and drug discovery because of their simplicity, efficiency, and high selectivity [27]. This environmentally friendly process can reduce the number of steps and synthesis of bioactive and complex molecules should be facile, fast, and efficient with minimal workup in this methodology [28-29]. Aza-containing heterocyclic compounds are widespread in nature, and their applications to pharmaceuticals, agrochemicals, and functional materials are becoming more and more important [30]. Among a large variety of N-containing heterocyclic compounds, those containing hydrazine moiety as 'fusion site' have received considerable attention because of their pharmacological properties and clinical applications [31]. Recently, several elegant multicomponent strategies for the synthesis of 2H-indazolo[2,1-b]phthalazine-triones and triazolo[1,2-a]indazole-triones by multi component reactions utilizing catalysts have been reported [32-40].

Experimental section:

Preparation of SBA-15-Ph-SO₃H:

To a 100 mL of round-bottom flask were introduced 30 mL of anhydrous toluene and 1.0 g of SBA-15 and 5 mL of dichlorodiphenylsilane (DCDPS) were added. The solution was refluxed for 12 hrs under an inert atmosphere; the solid was filtered and washed subsequently with toluene, dichloromethane, and methanol, and dried under reduced pressure at 60 °C for 12 h. Phenyl-modified SBA-15 was dispersed in dry Hexane (50 mL) under nitrogen and then trimethylsilylchloride (TMSCl, 3 mL) was added to the dispersion and for 8 h, cooled to r.t., filtered and washed with hexane to get the trimethylsilylated Phenyl-modified SBA-15. The dry white solid was soaked in the solution of ClSO₃H (0.6 mL) in dry CHCl₃ (20 mL) and the reactant was refluxing for 2 h. After filtrated and washed with dry CHCl₃, the solid was dried in vacuum at 60 °C for 10 h to obtain SBA-15 functionalized with phenyl sulfonic acid groups (Scheme1).

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
 ۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
 مجری: اهم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
 www.Processconf.ir



Scheme1.

General procedure for the synthesis of 2H-indazolo[2,1-b]phthalazine-triones and triazolo[1,2-a]indazole-triones in the presence of SBA-15-Ph-SO₃H under solvent-free conditions:

Phthalhydrazide (1 mmol), dimedone (1 mmol), aldehyde (1.1 mmol) and SBA-15-Ph-SO₃H (5 mol%, 20 mg) were heated at 80 °C. The reactions were followed by thin layer chromatography (TLC) using hexane/ethyl acetate (3:1) as an eluent ($R_f=0.70$). After completion of the reaction, the mixture was washed with ethyl acetate and filtered to recover the catalyst. The filtrate was evaporated, and the crude product was recrystallized from EtOH/H₂O (4:1) to afford pure products. The desired pure products were characterized by comparison of their physical data with those of known compounds. In order to recover the catalyst, the solid was washed with ethanol, ethyl acetate and dried. The recovered catalyst was reused another time.

Results and discussion:

Catalyst characterization:

SBA-15-Ph-SO₃H fabrication was confirmed by FT-IR (Fig 1). As it is seen in the curve **a**, the formation of SBA-15 structure is evidenced by the IR bands located at 3412 cm⁻¹ ($\nu_{as}O-H$), 1089 cm⁻¹ ($\nu_{as}Si-O$), 807 cm⁻¹ (ν_sSi-O), 468 cm⁻¹ ($\sigma Si-O-Si$) (ν represents stretching, σ bending, s symmetric, and as asymmetric vibration, Fig 1). The signals appeared at 2937 cm⁻¹ ($\nu C-H$ of benzyl), 1507 cm⁻¹ (ν benzene), 878 cm⁻¹ (σ benzene) and 855 cm⁻¹ (σ benzene) in curve **b** indicate the existence of benzene ring and successful attachment of dichlorodiphenylsilane to the

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
 ۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
 مجری: اهم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
 www.Processconf.ir

SBA-15. SBA-15-Ph-SO₃H exhibits additional diffraction peaks corresponding to sulfonic acid group in curve c. The characteristic peaks of sulfonic acid group are occurred at 1169 cm⁻¹ (νSO₂) and 574 cm⁻¹ (ν S-O). with was designed as SBA-15-Ph-SO₃H. The sulfonic content (the number of H⁺) of the catalyst based on CHN analysis and titration with NaOH is estimated to be 2.45 mmol/g.

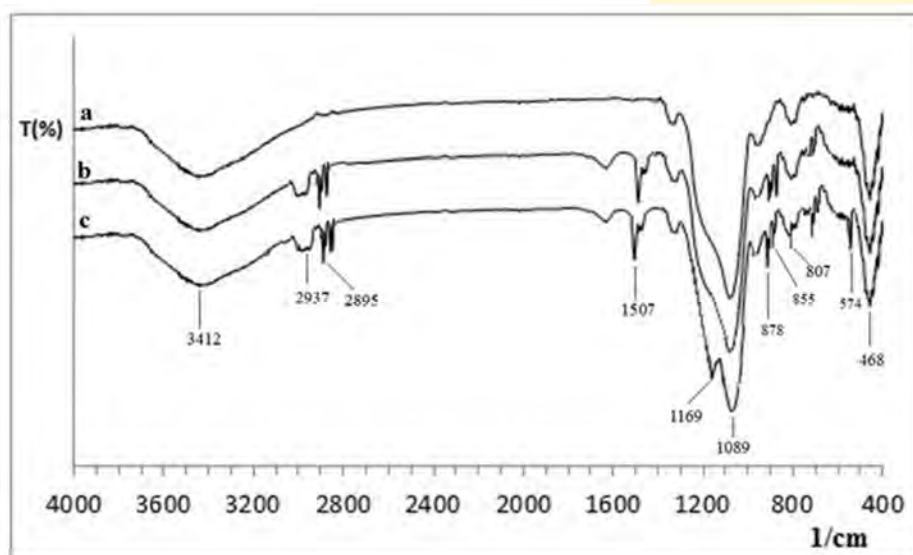


Fig. 1. FT-IR of the parent SBA-15, SBA-15-Ph and SBA-15-Ph-SO₃H

The structural elucidation of the SBA-15-Ph-SO₃H was performed in some details using TEM technique. TEM images of the catalyst (Fig. 2) show the ordered mesostructure in large domains and no distinct defect is observed.

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
 ۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
 مجری: احم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
 www.Processconf.ir

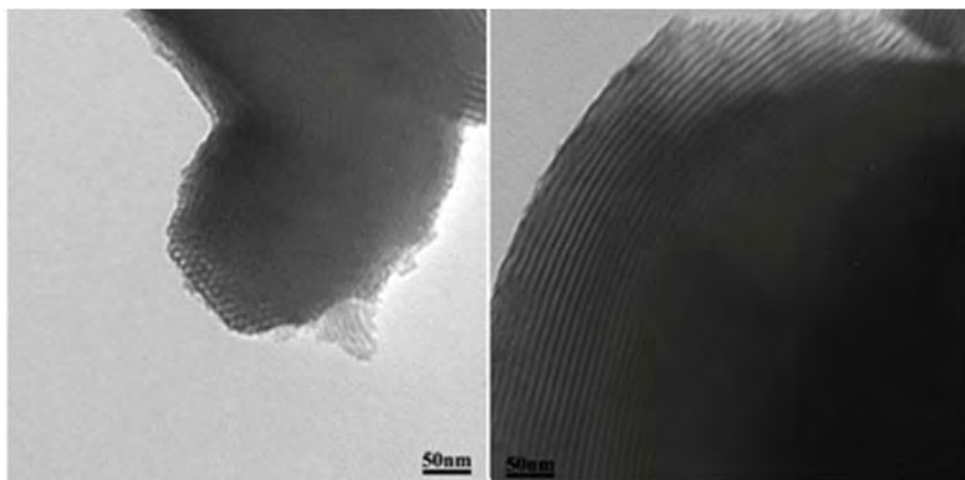


Fig. 2. TEM images of SBA-15-Ph-SO₃H

The small-angle XRD patterns for SBA-15 and SBA-15-Ph-SO₃H are shown in Fig. 2. Three well-resolved diffraction peaks in the 2θ range of $0.8-2^\circ$ are observed for the SBA-15-Ph-SO₃H as an organic-inorganic hybrid material like to SBA-15 parent. However, the ordered structure of SBA-15-Ph-SO₃H remained intact, which was supported by XRD results. This patterns feature distinct Bragg peaks in the 2θ range of $0.8-2^\circ$, which can be indexed as (1 0 0), (1 1 0) and (2 0 0) reflections of a two-dimensional hexagonal structure of SBA-15 material. The present of these peaks indicates that the crystallographic ordering of the mesopores in SBA-15-Ph-SO₃H is retained after grafted (Fig. 3).

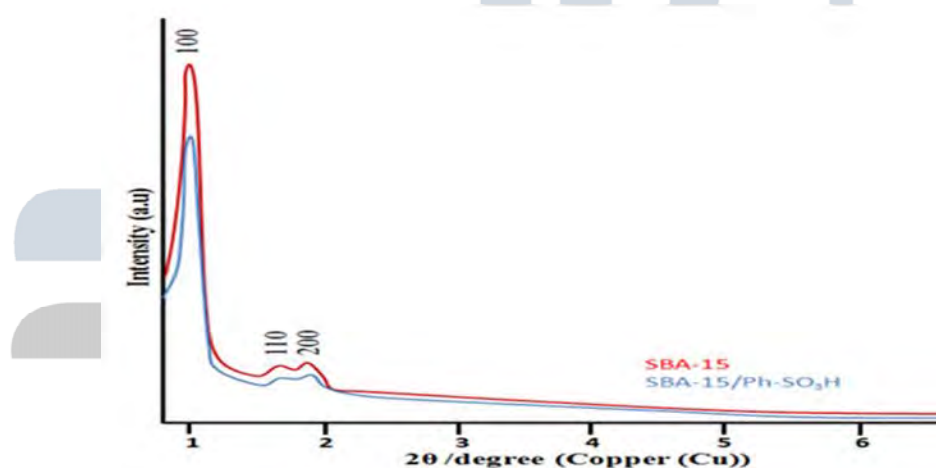


Fig. 3. XRD small angle patterns of the parent SBA-15, SBA-15-Ph-SO₃H

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
 ۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
 مجری: اهم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
 www.Processconf.ir

The generality of this reaction was examined using different aromatic and aliphatic aldehydes. The reactions proceeded smoothly and equally well for electron-withdrawing as well as electron-donating substituents on aldehydes to afford the corresponding phthalazine-triones in good to excellent yields (Table 1, entries 1-9) and in very short reaction times. This method offers significant improvements with regard to the scope of the transformation, simplicity, and green aspects by avoiding expensive or corrosive catalysts.

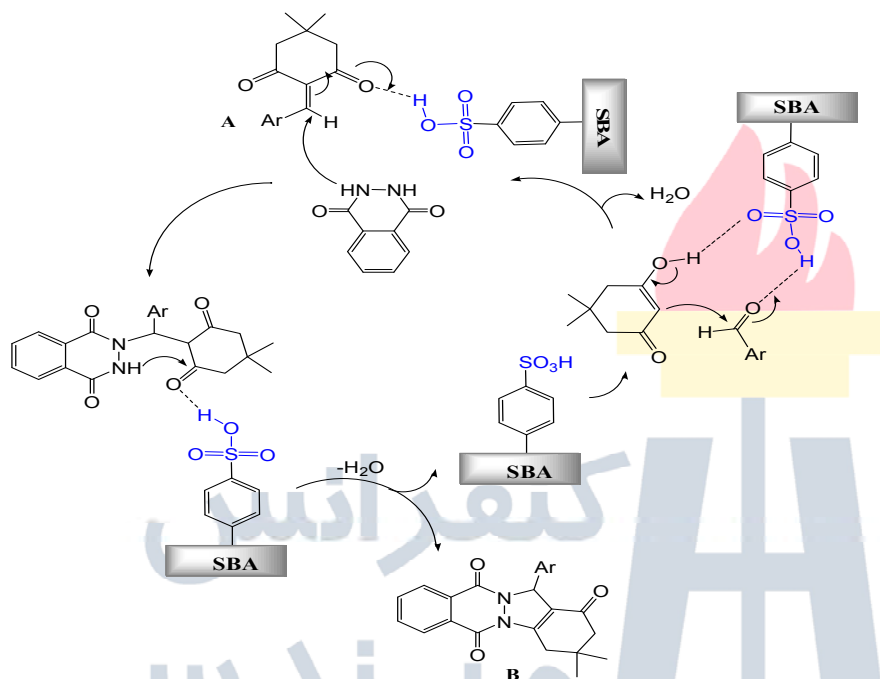
Table 1
 Synthesis of 2H-indazolo[2,1-b]phthalazine-triones in the presence of SBA-15-Ph-SO₃H

Entry	Aldehyde	Time (min)	Yield (%)	Mp (°C)	
				Found	Reported ^{lit.}
1	C ₆ H ₅	10	90	203-205	204-206 ⁴⁸
2	4-Cl-C ₆ H ₄	7	85	263-265	262-254 ⁵⁴
3	4-Br-C ₆ H ₄	5	95	264-266	265-267 ⁵⁵
4	4-MeO-C ₆ H ₄	5	96	217-219	218-220 ⁵⁵
5	3-NO ₂ -C ₆ H ₄	5	96	268-269	267-268 ⁵⁵
6	2,4-di-Cl-C ₆ H ₃	15	85	234-236	234-236 ⁵⁴
7	3,4,5-tri-MeO-C ₆ H ₂	10	95	187-189	188-190 ⁵⁸
8	Propanal	50	75	145-147	145-147 ⁵⁴
9	Butanal	45	80	135-137	136-138 ⁵⁴

^aKnown products were characterized from their physical properties, by comparison with authentic samples, and by spectroscopic methods.

The formation of 2H-indazolo[1,2-b]phthalazine-trione derivatives in the presence of SBA-15-Ph-SO₃H, which should be synthetically useful and practical, as presented in Scheme 2. A plausible pathway involves initial a SBA-15-Ph-SO₃H catalyzed Knoevenagel condensation of dimedone with aldehyde intermediate **A** was formed. Subsequent Michael addition of phthalhydrazideto intermediate **A** was occurred in the catalytic media, followed cyclization affords the corresponding product **B** in the catalytic cycle (Scheme 2).

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
 ۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
 مجری: احم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
 www.Processconf.ir



Scheme 2

The reusability of the catalyst in the reaction of 3-nitrobenzaldehyde, dimedone, and phthalhydrazide under solvent-free conditions at 80 ° C in 5 minute was studied. In this procedure, after completion of each reaction, hot ethylacetate was added to the reaction mixture and was shaken for a few minutes to dissolve the product. The catalyst (insoluble in solvent) was filtered and washed with hot ethanol and ethylacetate, and dried. The recovered catalyst was reused five times and smooth loss of catalytic activity was observed from the 5th time of reuse (Fig. 4).

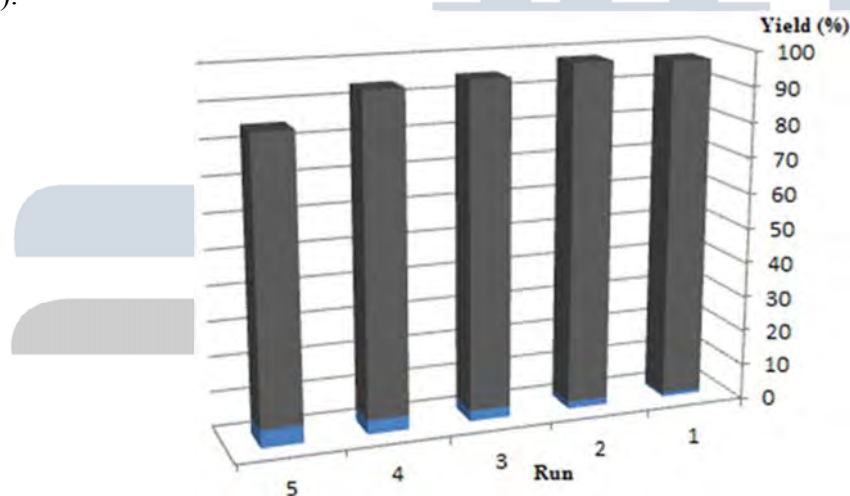


Fig. 4. The catalytic activity of SBA-15-Ph-SO₃H in five cycles for the reaction

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
مجری: اهم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
www.Processconf.ir

Conclusion:

In conclusion, we have prepared phenyl sulfonic acid functionalized mesoporous SBA-15 silica (SBA-15-Ph-SO₃H) as a novel hydrophobic nanoreactor solid acid catalyst, which was characterized. The sulfonic groups anchored to the silica surface of the pore walls are resistant to leaching in organic and aqueous solutions under mild conditions. This catalyst is found to be a recyclable heterogeneous catalyst for the rapid and efficient synthesis of various 2H-indazolo[2,1-b]phthalazine-triones. The catalyst has suitable hydrophobicity to drive out the water which is formed during the reaction from mesochannels.

Acknowledgement:

We are thankful to Iran National Science Foundation (INSF), Iranian Research Organization for Science and Technology (IROST) and Payame Noor University (PNU) for partial support of this work.

References:

- [1] F. Hoffmann, M. Cornelius, J. Morell, M. Fröba, *Angew. Chem. Int. Ed.* 45 (2006) 3216.
- [2] A. Stein, *Adv. Mater.* 15 (2003) 763.
- [3] H. Lee, S.I. Zones, M.E. Davis, *Nature* 425 (2003) 385.
- [4] M.E. Davis, *Nature* 417 (2002) 813.
- [5] X. Feng, G.E. Fryxell, L.Q. Wang, A.Y. Kim, J. Liu, K.M. Kemner, *Science* 276 (1997) 923.
- [6] Y. Mori, T.J. Pinnavaia, *Chem. Mater.* 13 (2001) 2173.
- [7] L. Mercier, T.J. Pinnavaia, *Adv. Mater.* 9 (1997) 500.
- [8] H. Yoshitake, *New J. Chem.* 29 (2005) 1107.
- [9] Q. Huo, D.I. Margolese and G.D. Stucky, *Chem. Mater.* 8 (1996) 1147.
- [10] S.L. Burkett, S.D. Sim, S. Mann, *Chem. Commun.* (1996) 1367.
- [11] L. Mercier, T.J. Pinnavaia, *Chem. Mater.* 12 (2000) 188.
- [12] D. Margolese, J.A. Melero, S.C. Christiansen, B.F. Chmelka, G.D. Stucky, *Chem. Mater.* 12 (2000) 2448.
- [13] R.D. Badley, W.T. Ford, *J. Org. Chem.* 54 (1989) 5437.
- [14] C.W. Jones, K. Tsuji, M.E. Davis, *Nature* 39 (1998) 352.
- [15] W.M. Van Rhijn, D.E. De Vos, B.F. Sels, W.D. Bossaert, P.A. Jacobs, *Chem. Commun.* (1998) 317.
- [16] M.H. Lim, C.F. Blanford, A. Stein, *Chem. Mater.* 10 (1998) 467.
- [17] W.D. Bossaert, D.E. De Vos, W.M. Van Rhijn, J. Bullen, P.J. Grobet, P.A. Jacobs, *J. Catal.* 18 (1999) 2156.
- [18] I. Diaz, C. Ma'riquez-Alvarez, F. Mohino, J. Pe'rez-Pariente and E. Sastre, *J. Catal.* 193 (2000) 283.

مجموعه مقالات چهارمین کنفرانس ملی مهندسی فرآیند، پالایش و پتروشیمی
۷ خرداد ۱۳۹۴، ایران، تهران، مرکز همایش‌های صدا و سیما
مجری: اهم اندیشان انرژی کیمیا ۸۸۶۷۱۶۷۶ - ۰۲۱
www.Processconf.ir

- [19] J.A. Melero, G.D. Stucky, R.V. Grieken, G. Morales, J. Mater. Chem. 12 (2002) 1664.
- [20] K. Wilson, J.H. Clark, Pure Appl. Chem. 72 (2000) 1313.
- [21] J. H. Clark, S. Elings, K. Wilson, C.R. Acad. Sci., Ser. IIC: Chim. 3 (2000) 399.
- [22] I. Diaz, F. Mohino, J. Pe´rez-Pariente, E. Sastre, Appl. Catal. 205 (2001) 19.
- [23] B. Lindlard, M. Lu´ chinger, M. Haouas, A. Kogelbauer, R. Prins, Stud. Surf. Sci. Catal. 135 (2001) 318.
- [24] J. Zhu, H. Bienayme, Multicomponent Reactions, Wiley-VCH, Weinheim, Germany, 2005.
- [25] A. Dömling, Chem. Rev. 106 (2006) 17-89.
- [26] D.F. Tejedor, G. Tellado, Chem. Soc. Rev. 36 (2007) 484.
- [27] A. Nefzi, J.M. Ostresh, R.A. Houghten, Chem. Rev. 97 (1997) 449.
- [28] L. Weber, Drug Dis. Today 7 (2002) 143.
- [29] A. Dömling, Curr. Opin. Chem. Bio. 6 (2000) 306.
- [30] V.P. Litvinov, Russ. Chem. Rev. 72 (2003) 69.
- [31] Clement, R.A. J. Org. Chem. 25 (1960) 1724.
- [32] M. Sayyafi, M. Seyyedhamzeh, H.R. Khavasi, A. Bazgir, Tetrahedron 64 (2008) 2375.
- [33] J.M. Khurana, M. Devanshi, Tetrahedron Lett. 50 (2009) 7300.
- [34] H.R. Shaterian, M. Ghashang, M. Feyzi, Appl. Catal. A: Gen. 345 (2008) 128.
- [35] E. Mosaddegh, A. Hassankhani, Tetrahedron Lett. 52 (2011) 488.
- [36] R. Fazaeli, H. Aliyan, N. Fazaeli, Open Catal. J. 3 (2010) 14.
- [37] G. Sabitha, C. Srinivas, A. Raghavendar, J.S. Yadav, Helv. Chim. Acta 93 (2010) 1375.
- [38] R. Ghorbani-Vaghei, R. Karimi-Nami, Z. Toghraei-Semiromi, M. Amiri, M. Ghavidel, Tetrahedron 67 (2011) 1930.
- [39] S. Gaurav, K.V. Rajiv, K.V. Girijesh, M. Shankar Singh, Tetrahedron Lett. 52 (2011) 7195.
- [40] W. Xiao, M. Wei-Wei, W. Li-Qiang, Y. Fu-Lin, J. Chin. Chem. Soc. 57 (2010) 1341.