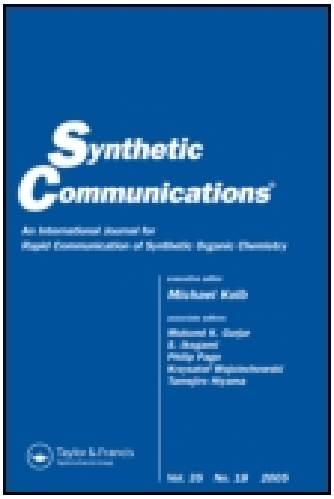

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Efficient and Ecofriendly Route for the Solvent-Free Synthesis of 4-Alkoxy-5H-chromen[2,3-d]pyrimidines Using Phosphonic Acid Functionalized KIT-6 Confined Ionic Liquid as Recoverable Catalyst

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EFFICIENT AND ECOFRIENDLY ROUTE FOR THE SOLVENT-FREE SYNTHESIS OF 4-ALKOXY-5*H*-CHROMEN[2,3-*d*]PYRIMIDINES USING PHOSPHONIC ACID FUNCTIONALIZED KIT-6 CONFINED IONIC LIQUID AS RECOVERABLE CATALYST

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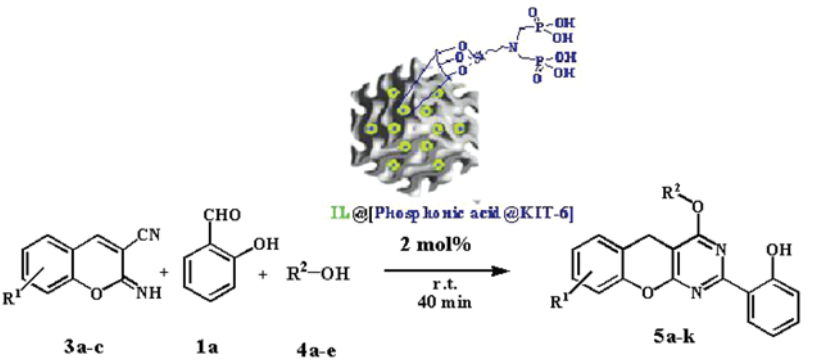
GRAPHICAL ABSTRACT



Abstract *Phosphonic acid functionalized KIT-6 confined ionic liquid (IL, 1-butyl-3-methylimidazolium tetrafluoroborate [BMIm][BF_4]) catalyzed the one-pot condensation reaction of iminochromenes and salicylaldehydes with different primary alcohols to achieve*

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the corresponding 4-alkoxy-5H-chromen[2,3-d]pyrimidines under solvent-free conditions and in good yields. This efficient nanocatalyst can be recovered for at least five reaction runs without significant loss of either activity or confined IL.

Keywords 4-Alkoxy-5*H*-chromen[2,3-*d*]pyrimidines; KIT-6 confined ionic liquid; one-pot synthesis; phosphonic acid functionalized KIT-6

INTRODUCTION

Multicomponent reactions (MCRs) have emerged as invaluable tools in the drug discovery process in a one-pot synthetic operation. MCRs include two or more steps without any isolation of intermediates, which reduce time and save both energy and raw materials.[1] These techniques permit fast, automated, economical, and high-throughput synthesis of the libraries of pharmaceutical and organic compounds.

Because of the diverse applications of the fluorescent compounds in biochemical and medical research,[2] new multicomponent synthetic approaches to obtain these compounds have received much attention. There are various synthetic strategies for the synthesis of pyrimidine derivatives,[3] some of which report the reaction of iminocoumarines in alcoholic solvents. In most of these reports, amines applied as nucleophiles and ultimately amino-5*H*-chromeno[2,3-*d*]pyrimidine-2-yl-phenols were obtained as major products. First, Costa and coworkers reported the synthesis of dimeric chromene derivatives via the condensation of salicylaldehyde and malononitrile in the CH_3OH and H_2O media.[4] They realized that during the dimerization process, CH_3OH as well as malononitrile attacked the intermediate as a nucleophile. According to our interest for the synthesis of pyrimidine derivatives, we tried to use alcohols as reactant for the synthesis of new pyrimidine derivatives. Therefore, due to the low nucleophylic property of alcohols, it was observed a suitable opportunity for solid acid catalysts. Recently $ZnCl_2$ was reported as a Lewis acid catalyst for the synthesis of 4-methoxy-5*H*-chromeno[2,3-*d*]pyrimidine derivatives.[5]

Recently, the utilization of ionic liquids (ILs) as green solvents for the laboratory as well as industrial applications has been reported. The favorable and unique properties such as low volatility, nonflammability, tunable polarity, miscibility with organic and inorganic compounds, and the ease of recycling process are the most important reasons for the widespread applications of ILs.[6] The most popular ILs are the incorporation of different alkylated imidazolium- or phosphonium-based cations with different anions such as tetrafluoroborate, hexafluorophosphate, etc.[7] In the past decade, the physiochemical properties of confined ILs within hybrid materials and their applications have been reported.[8] For example, a series of functionalized mesoporous silica confined ILs were prepared and applied as catalyst. The confinement effects studied and the results showed that filling meso-channels of mesoporous with ILs improved the catalyst performance and selectivity in different organic transformations. Over the past few years, the functionalized mesoporous silicas confined ILs have been reported as more efficient catalysts in different organic transformations.[9]

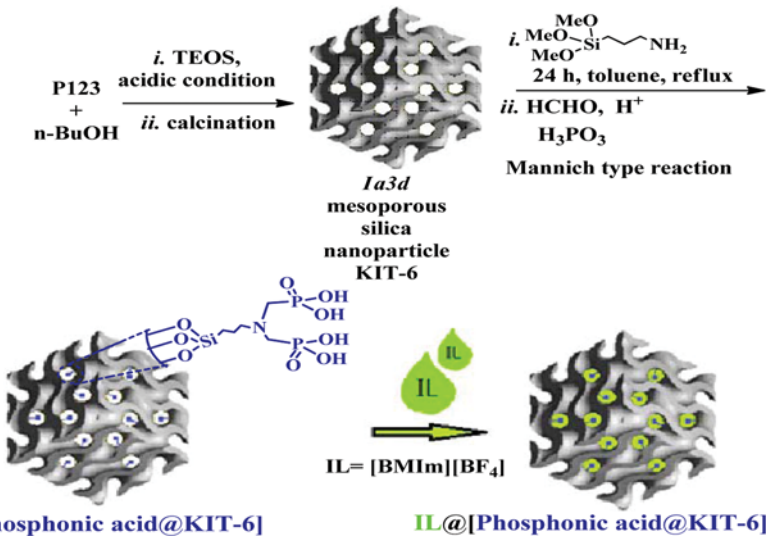
By virtue of the pivotal character of mesoporous silica nanoparticles (MSNs), they have increasingly proven to be an extremely effective support for the immobilization of a comprehensive range of homogeneous catalysts[10] and enzymes.[11] The

three-dimensional cubic *Ia3d* MSNs, having two interpenetrating continuous networks of chiral channels, provide highly opened nanoporous hosts with simple access for the guests and facilitating mass transfer through the channels.[12] KIT-6, composed of two interwoven nanochannels similar to that found in MCM-48,[13] was introduced as a promising candidate for the potential applications in hybrid catalyst generation and enzyme immobilization.[14,15] On the other hand, the relatively mild acidic behavior of phosphonic acid compared to stronger Brønsted acids such as H_2SO_4 may make it less prone to promotion of side reactions. Moreover, during recent years, phosphonic acid functionalized materials have been applied in the various fields such as bioelectrochemistry, electroanalysis, and biomimetic membranes.[16]

Following our previous research on multicomponent reactions and nanocatalysts,[17] it was of interest to investigate novel approaches for the synthesis of fluorescent chromenopyrimidine derivatives. Therefore, we report phosphonic acid functionalized KIT-6 confined ionic liquid [BMIm][BF_4], IL@[phosphonic acid@KIT-6], as a recoverable nanocatalyst and promoter for the green synthesis of 4-methoxy-5*H*-chromen[2,3-*d*] pyrimidine derivatives.

RESULTS AND DISCUSSION

In the present study, we designed and prepared KIT-6-functionalized phosphonic acid confined IL, IL@[phosphonicacid@KIT-6], as a promising candidate to catalyze different organic conversions. To this purpose, the silica framework KIT-6 has been synthesized via co-condensation of TEOS in the presence of the structure-directing agents under acidic conditions, and its surface was furnished by the covalent linkage of aminopropyl using 3-aminopropyl trimethoxysilane (APTMS).[18] Then phosphonic acid was incorporated into amine ends using



Scheme 1. Synthesis of [phosphonicacid@KIT-6] and IL@[phosphonicacid@KIT-6].

a straightforward Mannich-type reaction[19] between phosphorous acid and imine (from reaction between primary amine in aminopropyl functionalized KIT-6 and formaldehyde) in the presence of excess amount of concentrated HCl. Then the IL@[phosphonicacid@KIT-6] was prepared by filling the 3*D* mesochannels of phosphonic acid functionalized KIT-6 with [BMIm][BF_4] (Scheme 1).

The catalyst was comprehensively characterized by x-ray powder diffraction (XRD), N_2 adsorption–desorption analysis, Fourier transform–infrared (FT-IR), thermal gravimetric analysis (TGA), transmission electron microscopy (TEM), and scanning electron microscopy (SEM) (see the supplementary data). SEM and TEM recognize the ordered cubically honeycomb-like network with uniform mesochannels and morphology of the mesoporous solid KIT-6 (Fig. 1). The average pore diameter, which estimated from the TEM images, was about 7.5 nm, which agreed well with that from the N_2 sorption and XRD analysis.[19,20]

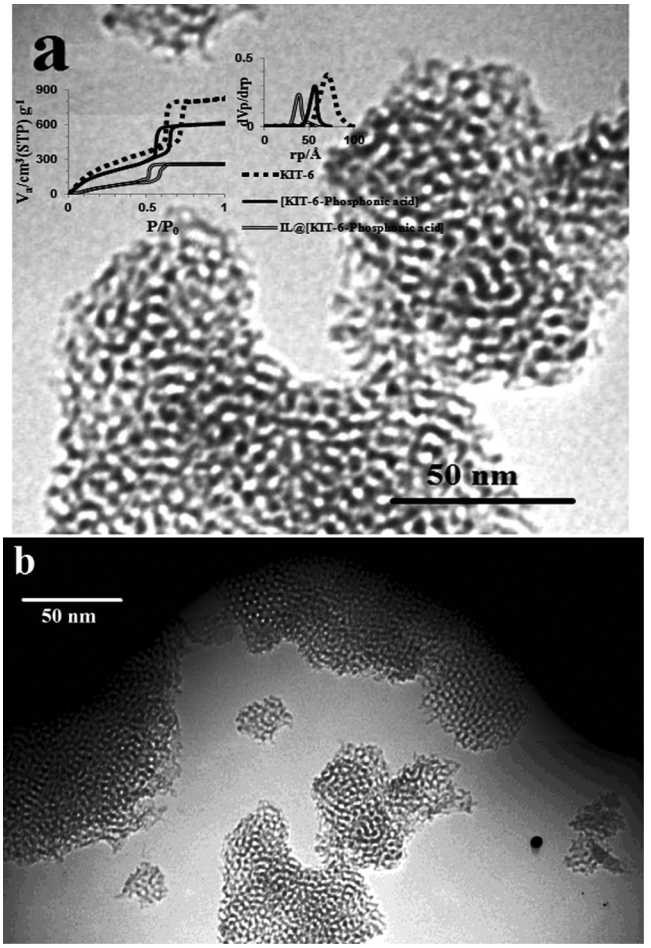
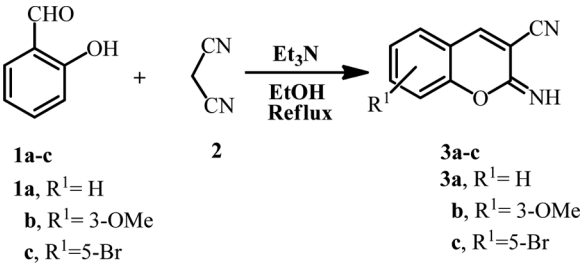


Figure 1. TEM image KIT-6 and N_2 sorption isotherm experiment of nanocatalyst in the subsequent modification process.



Scheme 2. Synthesis of iminochromenes (**3**) via tandem Knoevenagel and Pinner condensations.

Then the potential efficiency of [BMIm][BF_4]@[phosphonicacid@KIT-6] as an organic–inorganic nanohybrid catalyst was assessed in the synthesis of 4-alkoxy-5H-chromen[2,3-d]pyrimidines under different conditions. The catalytic performance and selectivity of [BMIm][BF_4]@[phosphonicacid@KIT-6] was evaluated in the synthesis of 4-methoxy-5H-chromen[2,3-d]pyrimidines via the three-component condensation between 2-imino-2H-chromene-3-carbonitrile, salicylaldehyde, and malononitrile as a model reaction. To this purpose, the required iminochromenes (**3a–c**) were prepared based on Knoevenagel condensation of salicylaldehydes (**1a–c**) and malononitrile (**2**) using the known procedure (Scheme 2).[21] To explore the generality of the present protocol, we applied various iminochromenes and alcohols, which led to a series of biologically interesting 4-alkoxy-5H-chromene[2,3-d]pyrimidines under optimum mild condition. Results are listed in Table 1.

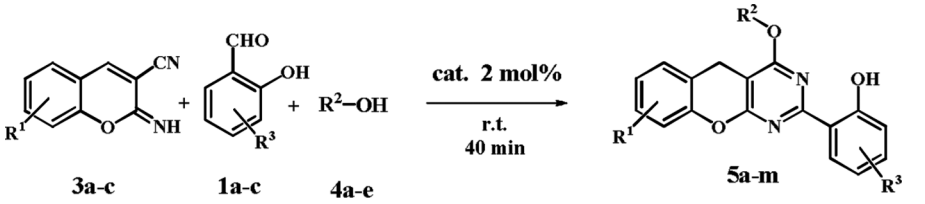
To illustrate the efficiency of this catalytic system, its ability was compared with different Lewis and Brønsted acids (Table 2). This clearly indicated that [BMIm][BF_4]@[phosphonicacid@KIT-6] could be introduced as the best catalyst for the aforementioned purpose. In a separate experiment, the use of [phosphonicacid@KIT-6] as a catalyst has worse results. This demonstrates the beneficial role of the ionic liquid in obtaining acceptable conversions.

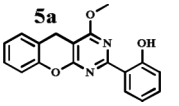
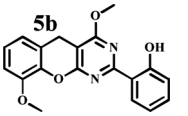
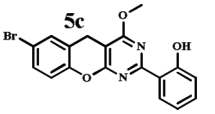
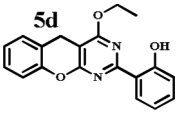
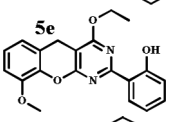
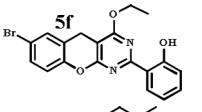
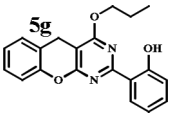
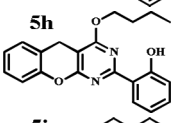
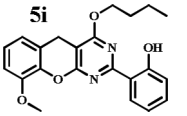
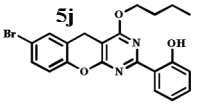
Based on the best of our knowledge, this investigation presents the first report of an ecosafe and efficient synthesis of 4-alkoxy-5H-chromene[2,3-d]pyrimidines. On the other hand, our method not only provides better yields in mild condition and reduced reaction times but also introduces recyclable Brønsted acid functionalized three-dimensional cubic *Ia3d* MSNs. Although the exact mechanism for the later reaction has not been established, it is reasonable to propose that product **5** results by nucleophilic attack of alcohol **4** to the obtained product **3** from the tandem Knoevenagel and Pinner reactions (Scheme 2) to produce intermediate **6**. Finally, the intermediate **6** reacted with salicylic aldehyde, followed by proton transfer to obtain the product **5** (Scheme 3).

Finally, to determine the applicability of catalyst recovery, the reaction mixture was filtered off and the remaining catalyst was washed to remove the probable residual product, dried under vacuum, and reused in subsequent runs. In five consecutive runs, the conversion stayed with no detectable loss (1st run: 90%, 1st reuse 89%, 2nd reuse: 90%, 3rd reuse: 88%, 4th reuse: 86%, Fig. 2), and the recovery yield of IL@[phosphonicacid@KIT-6] was more than 92%.

To explore the high potent and efficiency of this catalyst, we evaluated [BMIm][BF_4]@[phosphonicacid@KIT-6] as catalyst in the one-pot condensation

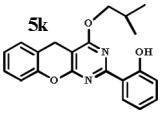
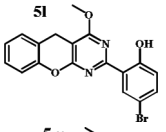
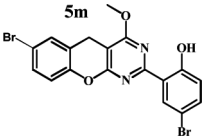
Table 1. Synthesis of 4-alkoxy-5*H*-chromen[2,3-*d*]pyrimidine derivatives



Entry	3	4	5	Yield (%)[a]
1	**3a**	**4a** CH_3OH	**5a** 	90
2	**3b**	**4a**	**5b** 	93
3	**3c**	**4a**	**5c** 	85
4	**3a**	**4b** CH_3CH_2OH	**5d** 	86
5	**3b**	**4b**	**5e** 	90
6	**3c**	**4b**	**5f** 	85
7	**3a**	**4c** $CH_3(CH_2)_2OH$	**5g** 	80
8	**3a**	**4d** $CH_3(CH_2)_3OH$	**5h** 	80
9	**3b**	**4d**	**5i** 	88
10	**3c**	**4d**	**5j** 	82

(*Continued*)

Table 1. Continued

Entry	3	4	5	Yield (%)[a]
11	**3a**	**4e** $(CH_3)_2CHCH_2OH$	**5k** 	85
13	**3a**	**4a**	**5l** 	89
14	**3c**	**4a**	**5m** 	83

[a]Yields refer to isolated pure products based on the reaction of **3(a–c)** (1 mmol), salicylaldehydes **1(a–c)** (1 mmol), alcohol **4(a–e)** (1.5 mmol), cat. (2 mol %), at rt and solvent-free conditions. The reaction mixture was stirred for 40 min. All known products have been reported in the literature, and they were characterized by comparing their melting points and NMR spectra with authentic samples.[5]

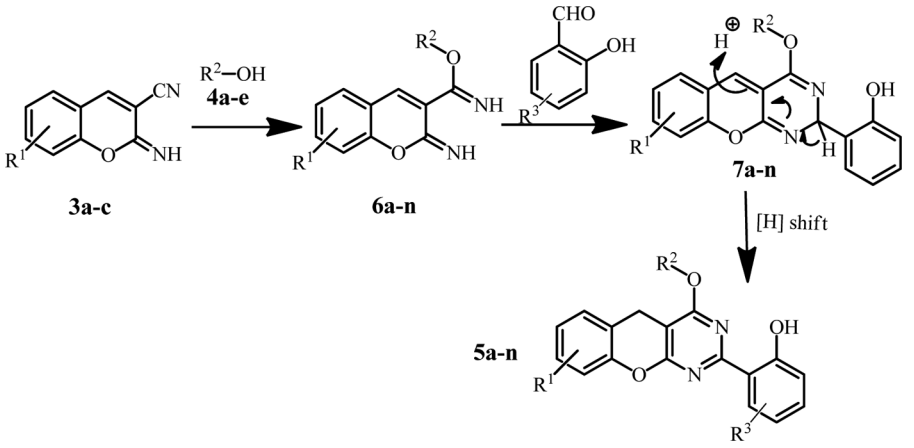
reaction of iminochromenes and salicylaldehyde with different amines to achieve the corresponding amino-5H-chromeno[2,3-d]pyrimidine-2-yl phenols. The reaction was accomplished in the presence of 1 mol% of [BMIm][BF_4]@[phosphonicacid@KIT-6] as catalyst under mild reaction condition and in good yields (Scheme 4).

In conclusion, we have successfully demonstrated phosphonic acid functionalized 3*D* cubic *Ia3d* KIT-6 confined [BMIm][BF_4] as a green, robust, and convenient reusable nanocatalyst for the synthesis of 4-alkoxy-5*H*-chromen[2,3-*d*]pyrimidine derivates under solvent-free conditions. Herein, 4-alkoxy-5*H*-chromen[2,3-*d*]pyrimidines was prepared via one-pot, three-component condensation of iminochromenes and salicylaldehyde with different primary alcohols under mild conditions and in excellent yields. Based on our observations, it could be concluded that good yields,

Table 2. Comparison of the efficiency of different catalyst in the model reaction

Entry	Catalyst	Condition[b]	Yield (%)
1	$ZnCl_2$	MeOH, rt	NR
2	$ZnCl_2$	MeOH, reflux	30
3	Fe_3O_4	MeOH, reflux	35
4	$AlCl_3$	MeOH, reflux	32
5	SiO_2	MeOH, reflux	40
6	$AlCl_3/SiO_2$	MeOH, reflux	45
7	$ZnCl_2/SiO_2$	MeOH, reflux	40
8	[Phosphonicacid@KIT-6]	Neat, rt	30
9	Free catalyst	[BMIm][BF_4], rt	40
10	IL@[Phosphonicacid@KIT-6][a]	Neat, rt	90

[a]IL = [BMIm][BF_4].
[b]The reactions run for 1 h.



Scheme 3. Proposed mechanism for the synthesis of 4-alkoxy-5*H*-chromen[2,3-*d*]pyrimidines **5**.

operational simplicity, practicability, and economical and environmental benefits are the worthy advantages of this protocol.

EXPERIMENTAL

Preparation of the Catalyst, IL@[Phosphonicacid@KIT-6]

The amine functionalized mesoporous silica KIT-6 ([n-PrNH_2-KIT-6]) was prepared according to the procedure reported in our previous article.[18] Then, as-synthesized [*n*-PrNH_2-KIT-6] (0.2 mol amine group), crystalline phosphorous acid (0.4 mol), and concentrated HCl (0.6 mol) were dissolved in 200 mL water, and the mixture was refluxed in a three-necked flask fitted with thermometer, condenser, and dropping funnel. During 1 h, 60 mL of a 40% (w/v) aqueous formaldehyde solution was added dropwise, and the reaction was refluxed for 1 h. The solvent was evaporated, and the concentrated residue was neutralized with concentrated ammonia solution. Finally, the obtained solid was filtered off, washed with hot dry MeOH for 12 h in a continuous extraction apparatus (Soxhelet), and then dried at 100 °C overnight to furnish the corresponding surface-bound phosphonic acid [phosphonicacid@KIT-6]. In the next step to achieve IL@[KIT-6-phosphonicacid],

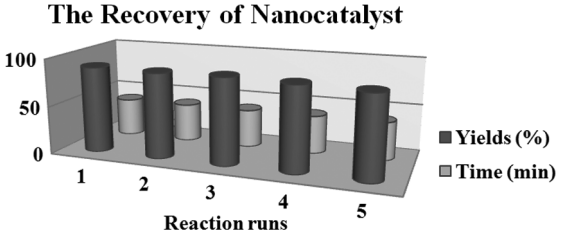
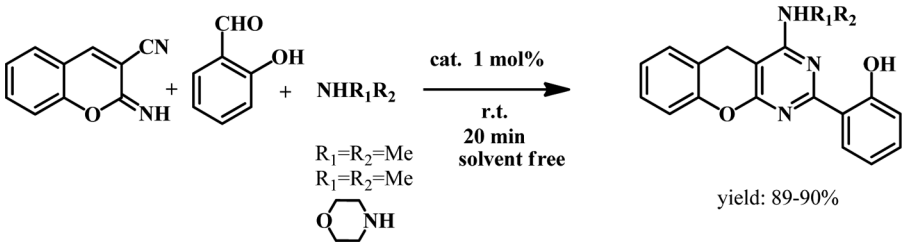


Figure 2. Recovery test of nanocatalyst for synthesis of **5a**.



Scheme 4. Synthesis of amino-5H-chromeno[2,3-*d*]pyrimidine-2-yl phenols.

1 g of [phosphonicacid@KIT-6] was added to a solution of 1-butyl-3-methylimidazolium tetrafluoroborate (3 mL) in dry acetone (50 mL). The reaction mixture was stirred at room temperature overnight. After stirring, acetone was removed under reduced pressure. The resulting solid was then dried at 70 °C under vacuum for 24 h, to obtain the designed catalyst IL@[KIT-6-phosphonicacid].

General Procedure for the Synthesis of 4-Methoxy-5H-chromen[2,3-*d*]pyrimidine

IL@[Phosphonicacid@KIT-6] catalyst (2 mol%) was added gently to a magnetically stirred mixture of iminocoumarine **3(a–c)** (1 mmol), salicylaldehyde **1a** (1 mmol), and alcohol **4(a–e)** (1.5 mmol). The reaction mixture was stirred for 40 min at room temperature. The progress of the reaction was monitored by thin-layer chromatography (TLC). When the spot for the product (Rf $\approx$ 0.8 in silica gel, EtOAc/n-hexane (1:5) was visible, the catalyst was separated by filtration or centrifuging, and the final product was purified by column chromatography using EtOAc/n-hexane 1:6 as an eluent and recrystallized from EtOH.

2-(4-Methoxy-5H-chromeno[2,3-*d*]pyrimidin-2-yl)phenol (5a)[4]

Colorless crystals; mp 198–200 °C (lit. mp 200 °C); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta_H = 3.97$ (s, 2H, CH_2), 4.18 (s, 3H, OCH_3), 6.97 (dt, $J = 7.5$, 1.0 Hz, 1H), 7.04 (dd, $J = 8.0$ Hz, 1H), 7.15 (dt, $J = 7.5$ Hz, 1.0 Hz, 1H), 7.19 (d, $J = 7.5$ Hz, 1H), 7.23–7.29 (m, 2H), 7.41 (dt, $J = 8.0$, 1.6 Hz, 1H), 8.46 (dd, $J = 8.0$, 1.6 Hz, 1H), 12.78 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta_C = 21.30$, 54.22, 94.41, 116.84, 117.31, 117.86, 118.43, 124.16, 127.76, 128.70, 128.75, 132.62, 136.81, 149.88, 159.78, 161.70, 167.14. Anal. calcd. for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.72; H, 4.90; N, 9.38.

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SUPPORTING INFORMATION

Full experimental details, ^{1}H and ^{13}C NMR spectra, and catalyst synthesis can be accessed on the publisher's website.

REFERENCES

1. (a) Zhu, J.; Bienaymé, H. *Multicomponent Reactions*; Wiley-VCH: Weinheim, Germany, 2005; (b) Orru, R. V. A.; Ruijter, E. *Synthesis of Heterocycles via Multicomponent Reactions I*; Springer: New York, 2010.
2. Lakowicz, J. R. *Principles of Fluorescence Spectroscopy*; Springer: New York, 2006; p. 63.
3. (a) Liu, J.; Wang, X. Microwave-assisted, divergent solution-phase synthesis of 1,3,6-trisubstituted pyrazolo[3,4-*d*]pyrimidines. *J. Comb. Chem.* **2011**, *13*, 414–420; (b) Dewen, L.; Shudong, D.; Youhong, H. Three-component, one-pot approach to synthesize benzopyrano[4,3-*d*]pyrimidines. *J. Comb. Chem.* **2010**, *12*, 895–899; (c) Georgescu, E.; Georgescu, F.; Popa, M. M.; Draghici, C.; Tarko, L.; Dumitrascu, F. Efficient one-pot, three-component synthesis of a library of pyrrolo[1,2-*c*]pyrimidine derivatives. *J. Comb. Chem.* **2012**, *14*, 101–107; (d) Borisov, A. V.; Dzhavakhishvili, S. G.; Zhuravel, I. O.; Kovalenko, S. M.; Nikitchenko, V. M. Parallel liquid-phase synthesis of benzopyrano[2,3-*d*]pyrimidine libraries. *J. Comb. Chem.* **2007**, *9*, 5–8.
4. Costa, M.; Areias, F.; Abrunhosa, L.; Venancio, A.; Proenca, F. The condensation of salicylaldehydes and malononitrile revisited: Synthesis of new dimeric chromene derivatives. *J. Org. Chem.* **2008**, *73*, 1954–1962.
5. Zonouzi, A.; Hosseinzadeh, F.; Karimi, N.; Mirzazadeh, R.; Ng, S. W. Novel approaches for the synthesis of a library of fluorescent chromenopyrimidine derivatives. *ACS Comb. Sci.* **2013**, *15*, 240–246.
6. (a) Wasserscheid, P.; Welton, T. *Ionic Liquid in Synthesis*; Wiley-VCH: Weinheim, Germany, 2008; (b) Zhao, D.; Wu, M.; Kou, Y.; Min, E. Ionic liquids: Applications in catalysis. *Catal. Today* **2002**, *74*, 157–189; (c) Favre, F.; Olivier-Bourbigou, H.; Commereuc, D.; Saussine, L. Hydroformylation of 1-hexene with rhodium in non-aqueous ionic liquids: How to design the solvent and the ligand to the reaction. *Chem. Commun.* **2001**, 1360–1361; (d) Dupont, J.; De Souza, R. F.; Suarez, P. A. Z. Ionic liquid (molten salt) phase organometallic catalysis. *Chem. Rev.* **2002**, *102*, 3667–3692.
7. (a) Dyson, P. J. Transition metal chemistry in ionic liquids. *Transition Met. Chem.* **2002**, *27*, 353–358; (b) Holbrey, J. D.; Seddon, K. R. Ionic liquids. *Clean Prod. Proc.* **1999**, *1*, 223–237; (c) Sheldon, R. Catalytic reactions in ionic liquids. *J. Chem. Soc., Chem. Commun.* **2001**, 2399–2407; (d) Zhao, H.; Malhotra, S. V. Applications of ionic liquids in organic synthesis. *Aldrichim. Acta* **2002**, *35*, 75–83; (e) Gordon, C. M. New developments in catalysis using ionic liquids. *Appl. Catal. A* **2001**, *222*, 101–117.
8. (a) Letaief, S.; Detellier, C. Nanohybrid materials from the intercalation of imidazolium ionic liquids in kaolinite. *J. Mater. Chem.* **2007**, *17*, 1476–1484; (b) Néouze, M. A.; Le Bideau, J.; Gaveau, P.; Bellayer, S.; Vioux, A. Ionogels, new materials arising from the confinement of ionic liquids within silica-derived networks. *Chem. Mater.* **2006**, *18*, 3931–3936; (c) Le Bideau, J.; Gaveau, P.; Bellayer, S.; Néouze, M. A.; Vioux, A. Effect of confinement on ionic liquids dynamics in monolithic silica ionogels: ^{1}H NMR study. *Phys. Chem. Chem. Phys.* **2007**, *9*, 5419–5422; (d) Chen, S.; Wu, G.; Sha, M.; Huang, S. Transition of ionic liquid [bmim][PF_6] from liquid to high-melting-point crystal when confined in multiwalled carbon nanotubes. *J. Am. Chem. Soc.* **2007**, *129*, 2416–2417.
9. (a) Zhang, J.; Zhang, Q.; Li, X.; Liu, S.; Ma, Y.; Shi, F.; Deng, Y. Nanocomposites of ionic liquids confined in mesoporous silica gels: Preparation, characterization, and

performance. *Phys. Chem. Chem. Phys.* **2010**, *12*, 1971–1981; (b) Karimi, B.; Vafaeezadeh, M. SBA-15-functionalized sulfonic acid confined acidic ionic liquid: A powerful and water-tolerant catalyst for solvent-free esterifications. *Chem. Commun.* **2012**, *48*, 3327–3329; (c) Karimi, B.; Badreh, E. SBA-15-functionalized TEMPO confined ionic liquid: An efficient catalyst system for transition-metal-free aerobic oxidation of alcohols with improved selectivity. *Org. Biomol. Chem.* **2011**, *9*, 4194–4198.

10. (a) Astruc, D.; Lu, F.; Aranzaes, J. R. Nanoparticles as recyclable catalysts: The frontier between homogeneous and heterogeneous catalysis. *Angew. Chem. Int. Ed.* **2005**, *44*, 7852–7872; (b) Narayanan, R. Recent advances in noble metal nanocatalysts for Suzuki and Heck cross-coupling reactions. *Molecules* **2010**, *15*, 2124–2138; (c) McNamara, C. A.; Dixon, M. J.; Bradley, M. Recoverable catalysts and reagents using recyclable polystyrene-based supports. *Chem. Rev.* **2002**, *102*, 3275–3299.
11. (a) Serra, E.; Mayoral, A.; Sakamoto, Y.; Blanco, R. M.; Diaz, I. Immobilization of lipase in ordered mesoporous materials: Effect of textural and structural parameters. *Micropor. Mesopor. Mater.* **2008**, *114*, 201–213; (b) Vinu, A.; Gokulakrishnan, N.; Balasubramanian, V. V.; Alam, S.; Kapoor, M. P.; Ariga, K.; Mori, T. Three-dimensional ultralarge-pore *Ia3d* mesoporous silica with various pore diameters and their application in biomolecule immobilization. *Chem. Eur. J.* **2008**, *14*, 11529–11538; (c) Lu, Y. J.; Guo, Y. L.; Wang, Y. Q.; Liu, X. H.; Wang, Y. S.; Guo, Y.; Zhang, Z. G.; Lu, G. Z. Immobilized penicillin G acylase on mesoporous silica: The influence of pore size, pore volume, and mesophases. *Micropor. Mesopor. Mater.* **2008**, *114*, 507–510; (d) Falahati, M.; Saboury, A. A.; Ma'mani, L.; Shafiee, A.; Rafieepour, H. A. The effect of functionalization of mesoporous silica nanoparticles on the interaction and stability of confined enzyme. *Int. J. Biolog. Macromol.* **2012**, *50*, 1048–1054.
12. (a) Corma, A. From microporous to mesoporous molecular sieve materials and their use in catalysis. *Chem. Rev.* **1997**, *97*, 2373–2419.
13. Pang, J.; Hampsey, J. E.; Hu, Q.; Wu, Z.; John, V. T.; Lu, Y. Mesoporous silica with *Ia3d* cubic structure and good thermal stability. *Chem. Commun.* **2004**, *6*, 682–683.
14. (a) Blanco, R. M.; Terreros, P.; Fernández-Pérez, M.; Otero, C.; Díaz-González, G. Functionalization of mesoporous silica for lipase immobilization: Characterization of the support and the catalysts. *J. Mol. Catal. B: Enzym.* **2004**, *30*, 83–93; (b) Lee, C.-H.; Lin, T.-S.; Mou, C.-Y. Mesoporous materials for encapsulating enzymes. *Nano Today* **2009**, *4*, 165–179; (c) Yiu, H. H. P.; Wright, P. A.; Botting, N. P. Enzyme immobilisation using siliceous mesoporous molecular sieves. *Micropor. Mesopor. Mater.* **2001**, *44–45*, 763–768.
15. Kleitz, F.; Choi, S. H.; Ryoo, R. Cubic *Ia3d* large mesoporous silica: Synthesis and replication to platinum nanowires, carbon nanorods, and carbon nanotubes. *Chem. Commun.* **2003**, *17*, 2136–2137.
16. (a) Zhang, F.; Zhou, Y.; Chen, Y.; Shi, Z. W.; Tang, Y. W.; Lu, T. H. Facile controlled preparation of phosphonic-acid-functionalized gold nanoparticles. *J. Colloid. Interfac. Sci.* **2010**, *351*, 421–426; (b) Davis, L. O.; Daniel, W. F. M.; Tobey, S. L. Phosphonic acid catalyzed synthesis of pyrazolidines. *Tetrahedron Lett.* **2012**, *53*, 522–525; (c) Lebed, P. J.; de Souza, K.; Bilodeau, F.; Larivière, D.; Kleitz, F. Phosphonate-functionalized large pore 3-D cubic mesoporous (KIT-6) hybrid as highly efficient actinide extracting agent. *Chem. Commun.* **2011**, *47*, 11525–11527.
17. (a) Jalili-Baleh, L.; Mohammadi, N.; Khoobi, M.; Ma'mani, L.; Foroumadi, A.; Shafiee, A. Synthesis of monospiro-2-amino-4*H*-pyran derivatives catalyzed by propane-1-sulfonic acid-modified magnetic hydroxyapatite nanoparticles. *Helv. Chim. Acta* **2013**, *96*, 1601–1609; (b) Ma'mani, L.; Heydari, A.; Sheykhan, M. The Ritter reaction under incredibly green protocol: Nano magnetically silica-supported Brønsted acid catalyst. *Appl. Catal. A: Gen.* **2010**, *384*, 122–127; (c) Ma'mani, L.; Sheykhan, M.; Heydari, A. Nanosilver embedded on hydroxyapatite-encapsulated γ-Fe_2O_3: Superparamagnetic catalyst for chemoselective

oxidation of primary amines to *N*-monoalkylated hydroxylamines. *Appl. Catal. A: Gen.* **2011**, *395*, 34–38.
18. Falahati, M.; Ma'mani, L.; Saboury, A. A.; Shafiee, A.; Foroumadi, A.; Badiei, A. R. Aminopropyl-functionalized cubic Ia3d mesoporous silica nanoparticle as an efficient support for immobilization of superoxide dismutase. *Biochim. Biophys. Acta* **2011**, *1814*, 1195–1202.
19. Punyacharoennon, P.; Charuchinda, S.; Srikulkit, K. Grafting and phosphonic acid functionalization of hyperbranched polyamidoamine polymer onto ultrafine silica. *J. Appl. Polym. Sci.* **2008**, *110*, 3336–3347.
20. Li, S.; Zhou, Z.; Abernathy, H.; Liu, M.; Li, W.; Ukai, J.; Hase, K.; Nakanishi, M. Synthesis and properties of phosphonic-acid-grafted hybrid inorganic–organic polymer membranes. *J. Mater. Chem.* **2006**, *16*, 858–864.
21. Rai, U. S.; Isloor, A. M.; Shetty, P.; Vijesh, A. M.; Prabhu, N.; Isloor, S.; Thiageeswaran, M.; Fun, H.-K. Novel chromeno [2,3-*b*]-pyrimidine derivatives as potential anti-microbial agents. *Eur. J. Med. Chem.* **2010**, *45*, 2695–2699.