available at www.sciencedirect.com

journal homepage: www.elsevier.com/locate/chnjc

Article (Special Issue for Excellent Research Work in Recognition of Scientists Who Are in Catalysis Field in China)

Silica-supported polycresulen as a solid acid catalyst for organic reactions

Kexing Zeng^{a,†}, Zhipeng Huang^{a,†}, Jie Yang^a, Yanlong Gu^{a,b,*}^a Key Laboratory for Large-Format Battery, Materials and System, Ministry of Education, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan 430074, Hubei, China^b State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Science, Lanzhou 730000, Gansu, China

ARTICLE INFO

Article history:

Received 25 April 2015

Accepted 22 May 2015

Published 20 September 2015

Keywords:

Acid catalysis

Solid acid

Polycresulen

Covalent bond-free immobilization

oxa-Pictet-Spengler reaction

ABSTRACT

A new type of solid catalyst was prepared by coating a thin layer of polycresulen, an inexpensive polymer prepared via condensation of 2-hydroxy-4-methylbenzenesulfonic acid and formaldehyde that has been used as commercially available drug, onto the surface of silica. The polycresulen component is insoluble in many organic solvents and can be adsorbed on silica with the aid of hydrogen bonding. The obtained silica/polycresulen composite showed remarkable catalytic activity for various organic reactions. In model reactions, the catalyst can be recycled several times without significant loss of activity. The salient features of using this acid catalyst in organic reactions include cost-effectiveness, simple and time-efficient preparation, and the convenience of controlling the acid loading on the solid.

© 2015, Dalian Institute of Chemical Physics, Chinese Academy of Sciences.

Published by Elsevier B.V. All rights reserved.

1. Introduction

Acid catalysts have been widely used in both academia and industry, and can be categorized into two major types: homogeneous liquid acids and heterogeneous solid acids [1–3]. Although homogeneous mineral acids, such as H₂SO₄ and HF, which are corrosive and toxic, have been widely adopted by chemical industry, with increasing pressure coming from environmental protection there is a need to develop green synthetic systems based on environmentally benign acid catalysts [4–8]. The use of heterogeneous solid acid catalysts has the general advantages of easier operation, milder conditions, reduced equipment corrosion, and minimized contamination of the

waste streams as well as reusability of the catalyst [9–11]. For this reason, heterogeneous solid acids have been extensively investigated [12–15], and in some chemical processes, their use has already contributed to significant improvement of both the synthetic efficiency and the greenness of the system [16–23]. Despite promising and sometime spectacular results, the practical application of solid acids in industrial processes is still hindered by many factors. Among all the methods used to prepare solid acids, the binding of catalysts to organic polymers or inorganic solids is widely used to produce a stable covalent bond between the acid center and the solid support, and is preferable to reduce the chance of leaching [24–26]. The synthesis of some solid acids with this method, however, involves

* Corresponding author. Tel: +86-027-87543032; Fax: +86-027-87544532; E-mail: klgyl@hust.edu.cn

[†] These authors contributed equally to this work

This work was supported by the National Natural Science Foundation of China (21173089, 21373093), the Fundamental Research Funds for the Central Universities of China (2014ZZGH019), and the Cooperative Innovation Center of Hubei Province.

DOI: 10.1016/S1872-2067(15)60910-X | http://www.sciencedirect.com/science/journal/18722067 | Chin. J. Catal., Vol. 36, No. 9, September 2015

several steps which are rather time-consuming. Furthermore, functionalization of a solid support using covalent bonds often requires harsh reaction conditions and as a consequence, calls for both a support and an acid precursor with sufficient chemical and thermal stability [27]. In many cases, a sophisticated operational procedure is also needed [28]. Therefore, some current solid acid catalysts are rather expensive and are therefore not widely used in synthesis. There thus exists a need to develop new, innovative approaches toward the design of recoverable and reusable solid acid catalysts.

Recently, the concept of solid-supported liquid phase catalysis has experienced a rekindled interest in the catalytic and synthetic community for the preparation of efficient heterogeneous catalytic materials [29–34]. With the aid of a thin layer of less volatile fluid coated onto the surface of solid support, some homogeneous catalysts have been easily immobilized without employing sophisticated operational procedures. In a selected reaction, solid form of the catalyst enables an easy recycling, but the reaction proceeded in microcosmically homogeneous conditions [35,36]. Inspired by this elegant strategy, we envision that it may be possible to transfer this concept to the development of a solid acid catalyst. To realize this idea, an acidic species that is amenable to the immobilization step and can stay stable on the surface of solid support is needed.

Policresulen is prepared by the condensation of metacresolsulfonic acid and formaldehyde and is commercially available as a clear red-brown solution. It is available at a low price in a number of countries worldwide [37]. Its systematic name is 2-hydroxy-3,5-bis(4-hydroxy-2-methyl-5-sulfobenzyl)-4-methylbenzenesulfonic acid. Policresulen is a topical hemostatic and antiseptic widely used as medicine for treating common anal disorders, such as hemorrhoids, and for gynecological infections [38]. Because the backbone of this reagent contains many hydroxyl and sulfonic acid groups, it is barely soluble in many organic solvents, such as toluene, ethyl acetate, and dichloroethane. The thermal stability and chemical stability of policresulen are quite good, making the extension of its applications to other fields possible. Considering that policresulen is a strong organic acid, and also taking into account its hydrophilic properties, we propose that it may be possible to con-

struct a new heterogeneous acid catalyst using this reagent as a homogeneous counterpart in conjunction with silica as a supporting material. Thus, we herein report a new solid acid composed of silica and policresulen that displays remarkable catalytic activity in many organic reactions. Compared with conventional solid acids, such as silica-supported sulfonic acid catalysts and Amberlyst-15, the materials obtained by our method have several advantages including simple and time-efficient preparation, low cost, and controllable sulfonic acid loading as well as tunable catalytic activity.

2. Experimental

2.1. Preparation of SiO_2 /policresulen composite catalysts **1a–1d**

In a typical procedure used to prepare silica/policresulen composite catalyst **1b**, silica gel (10 g) was added to a 250-mL round-bottomed flask containing a mixture of aqueous policresulen solution (52 wt%, 2.09 g) and ethanol (150 mL). The suspension was stirred at room temperature for 30 min prior to the removal of the ethanol and water under reduced pressure, affording free-flowing solid **1b**. Catalysts with different amounts of loaded policresulen (**1a**, **1c**, **1d**) were prepared in an analogous way.

2.2. Preparation of TiO_2 -supported benzenesulfonic acid catalyst **1f**

Titanium oxide (5 g) and toluene (100 mL) were added to a 250-mL round-bottomed flask equipped with magnetic stirring and a Dean-Stark apparatus. After 10 h of reflux, 4-hydroxybenzenesulfonic acid (3.87 g) dissolved in acetonitrile (7 mL) was added to the system and refluxed for another 16 h. At the end of the reaction, the solid was filtered, washed with ethanol (50 mL $\times$ 5) and dried under vacuum conditions, yielding catalyst **1f**. The ion exchange capacity of this catalyst was measured by titration. The obtained result was in good agreement with elemental analysis of the sulfur and carbon content.

Yanlong Gu (Huazhong University of Science and Technology) **received the Catalysis Rising Star Award in 2012**, which was presented by The Catalysis Society of China. Professor Yanlong Gu received his Ph.D. degree in Physical Chemistry from Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, in 2005. He then started a journey as post-doc researcher in the group of Prof. Shu Kobayashi, The University of Tokyo, Japan, and the group of Prof. Francois Jerome, The University of Poitiers, France. Since October 2008, Yanlong Gu become a professor in School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology. In 2009, he received an award of New Century Excellent Talents in Chinese Universities. He has a broad interest in homogeneous and heterogeneous catalysis, organic synthesis, biomass valorization and utilization. His research efforts are focusing on (1) catalysis with acids and ionic liquids; (2) green organic reactions for organic synthesis; and (3) eco-efficient processes based on utilization of biomass. He has published more than 80 research papers, 4 reviews in international peer review journals, and contributed two book chapters in the fields. H index of his publications reached 31 in 2015. Currently, he is a board member of Current Organic Chemistry and a committee member of ionic liquid division, Chemical Industry and Engineering Society of China.

2.3. Reactions

SiO₂/polycresulen composite catalyzed β -alkylation of styrene with benzhydrol. All reactions were conducted in a 10-mL V-type vessel equipped with a triangular magnetic stirrer. In a typical reaction, benzhydrol (92.1 mg, 0.5 mmol), styrene (62.4 mg, 0.6 mmol), and **1b** (20 mg, 2 mol%) were mixed in 1,2-dibromoethane (1.0 mL) and stirred for 5 h at 80 °C. After the reaction, the mixture was cooled to room temperature and petroleum ether (3.0 mL) was added prior to centrifugation. The liquid phase was subjected to isolation with PTLC (PE as eluent). The desired product, **4a**, was obtained in a yield of 92%. As for the solid phase, after washing with PE (3.0 mL $\times$ 3) and drying under vacuum, **1b** was used in the next run with a similar procedure. Tests of the substrate scope were conducted in the same manner.

SiO₂/polycresulen composite catalyzed oxa-Pictet-Spengler reaction. All reactions were conducted in a 10-mL V-type vessel equipped with a triangular magnetic stirrer. In a typical reaction, 2-(3,4-dimethoxyphenyl)ethanol (91.1 mg, 0.5 mmol), benzaldehyde (64.8 mg, 0.6 mmol), and **1b** (10 mg, 1 mol%) were mixed in 1,2-dichloroethane (1.0 mL) and stirred for 5 h at 80 °C. After the reaction, the mixture was cooled to room temperature and then centrifuged, and the liquid phase was subjected to isolation with PTLC (eluting solvent: ethyl acetate/petroleum ether = 1/8). The desired product, **7a**, was obtained in a yield of 96%. Tests of the substrate scope were conducted in the same manner. The recycling of **1b** was realized after doubling the dose. After washing the solid phase with PE (3.0 mL $\times$ 3) and drying under vacuum, the recovered **1b** was used in the next run with a similar procedure.

SiO₂/polycresulen composite catalyzed C3-alkenylation of 2-methylindoles with methyl acetoacetate. The reaction was conducted in a 10-mL V-type vessel equipped with a triangular magnetic stirrer. In a typical reaction, 2-methylindole (65.6, 0.5 mmol), methyl acetoacetate (116.1 mg, 1.0 mmol), and **1c** (50 mg, 10 mol%) were mixed in toluene (1.0 mL) and stirred for 16 h at 100 °C. After the reaction, the mixture was cooled to room temperature and then centrifuged, and the liquid phase was subjected to isolation with PTLC. The desired product, **10a**, was obtained in a yield of 90%. After washing the solid phase with PE (3.0 mL $\times$ 3) and drying under vacuum, the recovered **1c** was used in the next run with a similar procedure.

SiO₂/polycresulen composite catalyzed C3-alkenylation of 2-methylindole with phenylacetaldehyde. The reaction was conducted in a 10-mL V-type vessel equipped with triangle magnetic stirring. 2-methylindole (65.6, 0.5 mmol), phenylacetaldehyde (90.1 mg, 0.75 mmol), ethanol anhydrous (50.6 mg, 1.1 mmol) and **1d** (33.3 mg, 10 mol%) were mixed in dichloromethane (1.0 mL) and stirred for 11 h at room temperature. After reaction, petroleum ether (3.0 mL) was added prior to centrifuge, the liquid phase was submitted to isolation with PTLC. The desired product, **10b**, was obtained in a yield of 94%. After washing the solid phase with PE (3.0 mL $\times$ 3) and drying under vacuum, the recovered **1d** was used in the next run with a similar procedure.

2.4. Spectroscopic data of new compounds

(E)-1-chloro-4-(1-(4-methoxyphenyl)-3-phenylallyl)benzene (**4j**). Pale yellow liquid; ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.34 (d, J = 7.4 Hz, 2H), 7.27–7.23 (m, 3H), 7.19 (t, J = 2.7 Hz, 2H), 7.13 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 6.58 (dd, J_a = 7.3 Hz, J_b = 15.8, 1H), 6.29 (d, J = 15.9 Hz, 1H), 4.79 (d, J = 7.3 Hz, 1H), 3.75 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 158.4, 142.4, 137.2, 135.2, 132.4, 132.2, 131.6, 130.1, 129.6, 128.7, 127.5, 126.4, 114.1, 55.3, 52.8 ppm; HRMS m/z (ESI) calcd. for C₂₂H₁₉ClNaO [M + Na]⁺: 357.1022, found 357.1020.

(E)-1-fluoro-2-(1-(4-methoxyphenyl)-3-phenylallyl)benzene (**4k**). Pale yellow liquid; ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.36 (d, J = 7.4 Hz, 2H), 7.28 (t, J = 7.6 Hz, 2H), 7.22–7.12 (m, 5H), 7.10–7.00 (m, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.64 (dd, J_a = 7.2 Hz, J_b = 15.8 Hz, 1H), 6.31 (d, J = 15.8 Hz, 1H), 5.15 (d, J = 7.1 Hz, 1H), 3.76 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 161.9, 159.4, 158.3, 137.2, 134.4, 131.6, 131.4, 130.9, 130.8, 130.0, 129.9, 129.5, 128.6, 128.2, 128.1, 127.4, 126.4, 124.2, 124.1, 115.7, 115.5, 113.9, 55.3, 46.2, 46.2 ppm; HRMS m/z (ESI) calcd. for C₂₂H₁₉FNao [M + Na]⁺: 341.1318, found 341.1319.

(E)-1-chloro-2-(1-(4-methoxyphenyl)-3-phenylallyl)benzene (**4l**). Pale yellow liquid; ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.36–7.30 (m, 3H), 7.28–7.22 (m, 3H), 7.19–7.09 (m, 5H), 6.82 (d, J = 8.7 Hz, 1H), 6.59 (dd, J_a = 1.2 Hz, J_b = 15.9 Hz, 1H), 6.24 (d, J = 15.8 Hz, 1H), 5.33 (d, J = 6.6 Hz, 1H), 3.73 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 158.4, 141.3, 137.3, 134.3, 134.2, 131.9, 131.8, 130.2, 129.9, 128.7, 128.6, 127.9, 127.5, 127.0, 126.5, 113.9, 55.3, 49.5 ppm; HRMS m/z (ESI) calcd. for C₂₂H₁₉ClNaO [M + Na]⁺: 357.1022, found 357.1025.

(E)-1-chloro-4-(3-phenyl-1-(*p*-tolyl)allyl)benzene (**4m**). Pale yellow liquid; ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.33 (d, J = 7.2 Hz, 2H), 7.28–7.21 (m, 4H), 7.21–7.16 (m, 1H), 7.15–7.06 (m, 6H), 6.59 (dd, J_a = 7.4 Hz, J_b = 15.8 Hz, 1H), 6.30 (d, J = 15.8 Hz, 1H), 4.79 (d, J = 7.4 Hz, 1H), 2.30 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 142.4, 140.1, 137.2, 136.3, 132.3, 132.3, 131.7, 130.1, 129.4, 128.7, 128.6, 128.6, 127.5, 126.4, 53.3, 21.1 ppm; HRMS m/z (ESI) calcd. for C₂₂H₁₉ClNa [M + Na]⁺: 341.1073, found 341.1071.

6,7-Dimethoxy-1-phenethyl-isochroman (**7k**). Yellow liquid; ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.28 (t, J = 7.2 Hz, 2H), 7.22 (d, J = 6.0 Hz, 2H), 7.16 (tt, J_a = 1.6 Hz, J_b = 8.4 Hz, 1H), 6.58 (s, 1H), 6.52 (s, 1H), 4.70 (d, J = 6.4 Hz, 1H), 4.20–4.11 (m, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.78–3.71 (m, 1H), 2.98–2.86 (m, 1H), 2.83–2.71 (m, 2H), 2.65–2.56 (m, 1H), 2.23–2.01 ppm (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 147.5, 147.5, 142.4, 129.9, 128.5, 128.3, 126.1, 125.7, 111.5, 107.8, 74.8, 63.2, 56.0, 55.8, 37.8, 31.4, 28.6 ppm; HRMS m/z (ESI) calcd. for C₁₉H₂₂NaO₃ [M + Na]⁺: 321.1467, found 321.1465.

1-(4-Trifluoromethyl-phenyl)-1,3,4,9-tetrahydro-pyrano[3,4-b]indole (**7m**). Pale yellow liquid; ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.61 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 6.8 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 7.24–7.19 (m, 1H), 7.18–7.09 (m, 2H), 5.82 (s, 1H), 4.36–4.22 (m, 1H), 4.03–3.88 (m, 1H), 3.15–3.01 (m, 1H), 2.89–2.77 ppm (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 143.6, 136.3, 132.7, 131.3, 131.0, 130.0, 128.8, 128.4, 128.0, 127.0,

SiO₂-supported sulfonic acid catalyst **1e**. However, the obtained yield was far inferior to that obtained with **1b** (entry 6). To our surprise, although the acidic species of the TiO₂-supported benzenesulfonic acid catalyst **1f** has a similar molecular structure, a very low yield was obtained with this catalyst (entry 7). Although we are uncertain as to the reasons behind this discrepancy in performance, the poor catalytic activity of **1f** can be partially ascribed to insufficient contact between the catalyst and substrate, which is a result of the poor flexibility of the chemically bonded benzenesulfonic acid. A commonly used resin-supported acid, Amberlyst-15, was also examined, and only moderate yield was obtained under identical conditions (entry 8). These results indicate that silica/policresulen composites are indeed able to act as acid catalysts to promote organic reactions. Because the policresulen component is insoluble in DBE, the silica/policresulen composite catalyst **1b** could be recovered easily by filtration at the end of the reaction. After 20 min of treatment at 80 °C under vacuum conditions (10 mmHg), the recovered catalyst was subjected to the next run. With this procedure, **1b** could be reused at least four times without significant loss in its activity (entry 9). A congener of **1b** produced using toluenesulfonic acid (PTSA) as the acidic component (SiO₂-PTSA) was also used as a catalyst for the model reaction. Although good catalytic activity was obtained in the first run, its recyclability was far from satisfactory (entry 10). This result demonstrated that the policresulen component was key to rendering this immobilization protocol possible. Notably, the reaction could also be effectively scaled up by 10 times with similar efficiency (entry 11).

With the optimized conditions in hand, we probed the scope of the reaction with respect to both the styrene and the benzhydryl components. As evidenced by the results shown in Table 2, both electron-rich and moderately electro-poor styrenes reacted smoothly with benzhydryl, producing the substitution products in generally good to excellent yields. Styrene with methyl or phenyl at the α -position of the double bond was afforded with the aid of catalyst **1b** in moderate or excellent yield. The scope of the reaction with respect to the benzhydryl component was then investigated and was found to be good also. Several benzhydryl derivatives with methyl, methoxy, fluoro or chloro groups readily participated in the reaction with styrene, affording the corresponding tri-substituted ethylene in good to excellent yields.

Tertiary benzyl alcohols can undergo a dehydration reaction under acidic conditions to form styrene-type products [49]. Based on this mechanism, Han et al. [50] recently developed a tandem dehydration/nucleophilic substitution reaction involving two different alcohols. We found that this type of transformation can also be performed in our system with the aid of **1b**. As shown in Scheme 1, two benzhydryl-type alcohols reacted smoothly under the above-mentioned optimum conditions, providing the expected multi-substituted olefin **4h** in 96% yield, which is quite competitive compared with the result obtained for the condensation reaction of 1,1-diphenylethylene with benzhydryl over the same catalyst.

Encouraged by the promising results obtained in the above-mentioned reactions, we then applied the sili-

Table 2

Substrate scope of **1b**-catalyzed nucleophilic substitution of benzhydryls with styrenes.

Entry	Benzhydryl	Styrene	Time (h)	Product	Yield (%)
1	2a	3a	5	4a	92
2	2a	3b	5	4b	70
3	2a	3c	5	4c	50
4	2a	3d	5	4d	>99
5	2a	3e	7	4e	74
6	2a	3f	1.5	4f	>99
7	2a	3g	5	4g	75
8	2a	3h	1	4h	>99
9	2b	3a	15	4i	86
10	2c	3a	9	4j	92
11	2d	3a	5	4k	60
12	2e	3a	5	4l	90
13	2f	3a	5	4m	98

Reaction conditions: **2a** 0.5 mmol, **3a** 0.6 mmol, **1b** 2 mol%, DBE 1 mL, 80 °C.

Scheme 1. Tandem dehydration/nucleophilic substitution reaction of two different alcohols over catalyst **1b**.

ca/policresulen composite catalyst to the *oxa*-Pictet-Spengler reaction of 2-phenylethanol and benzaldehyde. This type of condensation relies heavily on the use of acid catalysts [51–55], and has been extensively used for the synthesis of isochromans. Although heterogeneous catalysts are preferable from the viewpoint of green chemistry, they are still rarely used in *oxa*-Pictet-Spengler reactions. Until now, there has been only one report on the use of a solid catalyst, a small pore size zeolite Ersorb-4 [56]. This is a clinoptilolite-type zeolite material with high Si content (Si:Al ratio 5:1). Unfortunately, this kind of zeolite is inaccessible to most labs working in organic chemistry. We found that, in the presence of a catalytic amount of **1b**, 2-(3,4-dimethoxyphenyl)ethanol **5a** reacted readily in 1,2-dichloroethane with benzaldehyde **6a** at 80 °C, affording the expected isochroman **7a** in 96% yield after 5 h (Table 3, entry 1). In this reaction, catalyst **1b** could also be recycled at least three times without significant loss in activity. Increasing

Table 3*Oxa*-Pictet-Spengler reaction catalyzed by solid acid catalysts.

Entry	Alcohol	R ³	Product	Catalyst	Time (h)	Yield (%)
1	5a	C ₆ H ₅	7a	1b	5	96(95 ^a , 93 ^b)
2	5a	C ₆ H ₅	7a	1e	5	78
3	5a	C ₆ H ₅	7a	1f	5	41
4	5a	4-MeOC ₆ H ₄	7b	1b	12	88
5	5a	2-MeOC ₆ H ₄	7c	1b	5	90
6	5a	4-NO ₂ C ₆ H ₄	7d	1b	3	98
7	5a	2-NO ₂ C ₆ H ₄	7e	1b	3	98
8	5a	4-ClC ₆ H ₄	7f	1b	5	97
9	5a	2-ClC ₆ H ₄	7g	1b	5	96
10	5a	4-BrC ₆ H ₄	7h	1b	3	98
11	5a	4-CNC ₆ H ₄	7i	1b	5	>99
12	5a	H	7j	1b	5	93
13	5a	C ₆ H ₅ (CH ₂) ₂	7k	1b	16	98
14	5b	C ₆ H ₅	7l	1b	16	91
15	5c	4-CF ₃ C ₆ H ₅	7m	1b	36	75

Reaction conditions: alcohol 0.5 mmol, aldehyde 0.6 mmol, 1,2-dichloroethane 1.0 mL, 80 °C, 5 h. ^a **1b** was reused in the third run. ^b reaction scale 5.0 mmol.

the reaction scale from 0.5 to 5.0 mmol did not significantly influence the synthetic efficiency. However, when SiO₂-supported sulfonic acid **1e** was used as catalyst, the yield of **7a** reached only 78% (entry 2). The reaction with TiO₂-supported benzenesulfonic acid catalyst **1f** proceeded sluggishly, affording **7a** in only 41% under identical conditions (entry 3).

Subsequently, other aldehydes and alcohols were subjected to the conditions used for entry 1 (Table 3). First, we selected a set of aldehydes spanning a convenient spectrum of lipophilicity and reactivity and used **5a** as the only source of the required alcohol. When **1b** was used as the catalyst, the results for all the aldehydes, which included both aromatic and aliphatic aldehydes, largely paralleled those obtained with benzaldehyde (entries 4–13). The reaction appeared to be insensitive to the presence of a substituent in the C2 position of benzaldehyde; 2-methoxybenzaldehyde, 2-nitrobenzaldehyde, and 2-chlorobenzaldehyde reacted as well as their C4-substituted congeners (entries 4–9). Under the present conditions, a cyano group could be delivered into the final product without any structural damage (entry 11). 3-Methoxyphenethyl alcohol **5b**

and tryptophol **5c** could also be used as counter substrates of the aldehyde component. Thus, catalyst **1b** was proved again to be effective for these *oxa*-Pictet-Spengler reactions (entries 14 and 15).

The silica/policresulen composite catalyst was also used in the 3-alkenylation of indoles with 1,3-dicarbonyl compounds, which can produce valuable C3-substituted indoles. The use of some Lewis or Brønsted acids, such as FeCl₃ [57], I₂ [58], acidic ionic liquid [59], and an Au (III) salt catalyst [60] has been examined for this reaction. However, all these catalysts are homogeneous and cannot be recycled. Using **1c** as the catalyst, 2-methylindole **8a** reacted smoothly with methyl acetoacetate **9a** in toluene, affording the corresponding C3-alkenylated indole **10a** in 90% yield (Scheme 2). At the end of the reaction, catalyst **1c** was easily recovered and reused at least two times without significant loss in activity. It should be noted that the same reaction over silica-supported sulfonic acid catalyst **1e** failed to give a satisfactory result. Because only 55% yield was obtained with catalyst **1b** under identical conditions, we deduced that the reaction might be significantly influenced by the catalyst loading. Fortunately, it is very easy to increase the loading of the policresulen component on the present catalyst. In contrast, an increase in acid loading with the conventional silica-supported sulfonic acid catalyst is not easy because it generally needs a sophisticated procedure and strict control of the preparation parameters. 2-Methylindole can also readily undergo an alkenylation with 2-phenylacetaldehyde over **1d** (Scheme 2). A similar reaction using FeCl₃ as the catalyst has been reported by Yang et al. [61]. An excellent yield, 94%, was obtained after 11 h of stirring at room temperature. In this reaction, the recovered **1d** also showed good recyclability. We have thus established the first heterogeneous catalytic system for 3-alkenylation of indoles with 1,3-dicarbonyl compounds and 2-phenylacetaldehyde.

4. Conclusions

Conventional methods for heterogenizing homogeneous molecular catalysts must covalently anchor the desired catalyst molecule on a solid support, and are thus rather complex and sometimes need sophisticated operations. The present silica/policresulen system achieves the ultimate goal for moving from a homogeneous catalyst towards heterogeneous conditions: easy separation of the catalyst and products while maintaining the same activity. The distinction in our case is that the catalytically active component, policresulen, could be easily immobilized on silica without forming chemical bonds. The unique structure of policresulen is the key factor that renders this protocol possible. The hydroxyl groups of policresulen

Scheme 2. C3-Alkenylation of 2-methylindole over silica/policresulen composite catalyst.

likely enable the formation of hydrogen bonds that facilitate its immobilization, while the sulfonic acid ensures a good catalytic activity of the composite. This catalyst exhibited good performance in various organic reactions, including β -alkylation of styrenes with benzhydrol, *oxa*-Pictet-Spengler reactions, and C3-alkenylation of indoles with 1,3-dicarbonyl compounds. However, we wish to point out that the catalytic reaction might occur in a homogeneous aqueous phase formed at the surface of the silica, and that the use of an organic solvent that cannot dissolve the polycresulen component allows the catalyst to remain stable on the solid component. Because this unique composite catalyst can be easily prepared without the use of any special instruments, researchers working in both catalytic reaction and organic synthesis may find it of use in the future. We are actively working on exploration of other reactions with this catalyst with the hope of clarifying its application scope and limitations.

References

- [1] Clark J H, Macquarrie D J. *Handbook of Green Chemistry and Technology*. Oxford: Wiley-Blackwell, 2002. 86
- [2] Tatsumi T, Sheldon R A, Van Bekkum H. *Fine Chemicals Through Heterogeneous Catalysis*. New York: Wiley-VCH, 2001. 185
- [3] Akiyama T. *Chem Rev*, 2007, 107: 5744
- [4] Corma A, Garcia H. *Chem Rev*, 2003, 103: 4307
- [5] Busca G. *Chem Rev*, 2007, 107: 5366
- [6] Kozhevnikov I V. *J Mol Catal A*, 2007, 262: 86
- [7] Kobayashi S, Manabe K. *Pure Appl Chem*, 2000, 72: 1373
- [8] Pan X J, Li M H, Gu Y L. *Chem Asian J*, 2014, 9: 268
- [9] Corma A. *Curr Opin Solid State Mater Sci*, 1997, 2: 63
- [10] Tanabe K, Holderich W F. *Appl Catal A*, 1999, 181: 399
- [11] Corma A, Garcia H. *Catal Today*, 1997, 38: 257
- [12] Song X, Sayari A. *Catal Rev-Sci Eng*, 1996, 38: 329
- [13] Corma A. *Chem Rev*, 1995, 95: 559
- [14] Kozhevnikov I V. *Chem Rev*, 1998, 98: 171
- [15] Lotero E, Liu Y, Lopez D E, Suwannakarn K, Bruce D A, Goodwin J G Jr. *Ind Eng Chem Res*, 2005, 44: 5353
- [16] Vilcoq L, Castilho P C, Carneiro F, Duarte L C. *ChemSusChem*, 2014, 7: 1010
- [17] Melero J A, Iglesias J, Morales G. *Green Chem*, 2009, 11: 1285
- [18] Rinaldi R, Schueth F. *ChemSusChem*, 2009, 2: 1096
- [19] Cejka J, Wichterlova B. *Catal Rev-Sci Eng*, 2002, 44: 375
- [20] Zabeti M, Daud W M A W, Aroua M K. *Fuel Proc Technol*, 2009, 90: 770
- [21] Wilson K, Clark J H. *Pure Appl Chem*, 2000, 72: 1313
- [22] Pastor I M, Yus M. *Curr Org Chem*, 2007, 11: 925
- [23] Vaidya T, Eisenberg R, Frontier A J. *ChemCatChem*, 2011, 3: 1531
- [24] Nakajima K, Hara M. *ACS Catal*, 2012, 2: 1296
- [25] Harmer M A, Sun Q. *Appl Catal A*, 2001, 221: 45
- [26] Salehi P, Ali Zolfigol M, Shirini F, Baghbanzadeh M. *Curr Org Chem*, 2006, 10: 2171
- [27] Okuhara T. *Chem Rev*, 2002, 102: 3641
- [28] Brunel D, Blanc A C, Galarneau A, Fajula F. *Catal Today*, 2002, 73: 139
- [29] Van Doorslaer C, Wahlen J, Mertens P, Binnemans K, De Vos D. *Dalton Trans*, 2010, 39: 8377
- [30] Steinrueck H P, Wasserscheid P. *Catal Lett*, 2015, 145: 380
- [31] Werner S, Szesni N, Kaiser M, Haumann M, Wasserscheid P. *Chem Eng Technol*, 2012, 35: 1962
- [32] Gu Y L, Li G X. *Adv Synth Catal*, 2009, 351: 817
- [33] Zhao F, Fujita S J, Arai M. *Curr Org Chem*, 2006, 10: 1681
- [34] Riisager A, Fehrmann R, Haumann M, Wasserscheid P. *Eur J Inorg Chem*, 2006: 695
- [35] Riisager A, Fehrmann R. *Ionic Liquids in Synthesis*. 2nd Ed. New York: Wiley-VCH, 2008. 527
- [36] Tundo P, Perosa A, Zecchini F. In: Perosa A, Zinovyev S ed. *Methods and Reagents for Green Chemistry*. New York: John Wiley & Sons, 2007. 131
- [37] Kilmarx P H, Limpakarnjanarat K, Supawitkul S, Korattana S, Young N L, Parekh B S, Respass R A, Mastro T D, St Louis M E. *AIDS*, 1998, 12: 767
- [38] Marrero-Ponce Y, Meneses-Marcel A, Castillo-Garit J A, Machado-Tugores Y, Escario J A, Barrio A G, Pereira D M, Nogal-Ruiz J J, Aran V J, Martinez-Fernandez A R, Torrens F, Rotondo R, Ibarra-Velarde F, Alvarado Y J. *Bioorg Med Chem*, 2006, 14: 6502
- [39] Gu Y L, Azzouzi A, Pouilloux Y, Jerome R, Barrault J. *Green Chem*, 2008, 10: 164
- [40] Sun S H, Bai R X, Gu Y L. *Chem Eur J*, 2014, 20: 549
- [41] Kamegawa T, Matsuura S, Seto H, Yamashita H. *Angew Chem Int Ed*, 2013, 52: 916

Graphical Abstract

Chin. J. Catal., 2015, 36: 1606–1613 doi: 10.1016/S1872-2067(15)60910-X

Silica-supported polycresulenes as a solidacid catalyst for organic reactions

Kexing Zeng, Zhipeng Huang, Jie Yang, Yanlong Gu*
Huazhong University of Science and Technology;
Lanzhou Institute of Chemical Physics, Chinese Academy of Science

A new type of solid catalyst was prepared by coating a thin layer of polycresulen, a commercially available drug, onto the surface of silica. The obtained silica/polycresulen composite showed remarkable catalytic activity for various organic reactions.

Salient features: low cost; easy to prepare; high efficiency; good recyclability and diverse applications in catalysis.

- [42] Notestein J M, Iglesia E, Katz A. *Chem Mater*, 2007, 19: 4998
- [43] Yue H L, Wei W, Li M M, Yang Y R, Ji J X. *Adv Synth Catal*, 2011, 353: 3135
- [44] Liu Z Q, Zhang Y, Zhao L, Li Z, Wang J, Li H, Wu L M. *Org Lett*, 2011, 13: 2208
- [45] Huang G B, Wang X, Pan Y M, Wang H S, Yao G Y, Zhang Y. *J Org Chem*, 2013, 78: 2742
- [46] Kumar R, Van der Eycken E V. *Chem Soc Rev*, 2013, 42: 1121
- [47] Emer E, Sinisi R, Capdevila M G, Petruzzello D, De Vincentiis F, Cozzi P G. *Eur J Org Chem*, 2011, 4: 647
- [48] Aoyama T, Koda S, Takeyoshi Y, Ito T, Takidoa T, Kodomari M. *Chem Commun*, 2013, 49: 6605
- [49] Gu Y L, Karam A, Jerome F, Barrault J. *Org Lett*, 2007, 9: 3145
- [50] Han F, Yang L, Li Z, Zhao Y, Xia C. *Adv Synth Catal*, 2014, 356: 2506
- [51] Saito A, Takayama M, Yamazaki A, Numaguchi J, Hanzawa Y. *Tetrahedron*, 2007, 63: 4039
- [52] Saeed A. *Chin Chem Lett*, 2010, 21: 261
- [53] Bouguerne B, Hoffmann P, Lherbet C. *Synth Commun*, 2010, 40: 915
- [54] Lherbet C, Soupaya D, Baudoin-Dehoux C, André C, Blonski C, Hoffmann P. *Tetrahedron Lett*, 2008, 49: 5449
- [55] Li M H, Taheri A, Liu M, Sun S H, Gu Y L. *Adv Synth Catal*, 2014, 356: 537
- [56] Hegedus A, Hell Z. *Org Biomol Chem*, 2006, 4: 1220
- [57] Yadav J S, Subba Reddy B V, Praneeth K. *Tetrahedron Lett*, 2008, 49: 199
- [58] Singh N, Singh K N. *Synlett*, 2012, 23: 2116
- [59] Santra S, Majee A, Hajra A. *Tetrahedron Lett*, 2011, 52: 3825
- [60] Arcadi A, Alfonsi M, Bianchi G, D'Annibale G, Marinelli F. *Adv Synth Catal*, 2006, 348: 331
- [61] Yang Q, Wang L D, Guo T L, Yu Z K. *J Org Chem*, 2012, 77: 8355

SiO₂负载聚甲酚磺醛作为固体酸催化剂用于有机反应

曾科星^{a,†}, 黄志鹏^{a,†}, 杨 杰^a, 顾彦龙^{a,b,*}

^a华中科技大学化学与化工学院, 教育部大型电池关键材料与系统重点实验室, 湖北武汉430074

^b中国科学院兰州化学物理研究所, 羰基合成与选择氧化国家重点实验室, 甘肃兰州730000

摘要: 均相催化多相化是催化化学研究热点之一。但是, 很多固体催化剂的制备需要专门的仪器设备和长期的实验技术积累, 而一般的有机合成化学实验室并不具备制备和调控固体催化剂的条件。另外, 部分固体催化剂制备过程较为复杂, 制备周期较长, 因此, 人们在进行有机转化反应操作时往往倾向于采用均相催化剂。为了改变这一现状, 需要尽快发展制备方法简单、周期短、性能可靠的固体催化剂, 以期能够在当前化学反应绿色化过程中做出更大贡献。

酸催化剂广泛用于有机合成反应。传统硫酸、氢氟酸等均相酸催化剂虽然催化活性较好, 但其腐蚀性强、毒性大, 且回收困难。为了提高化学转化过程的绿色性, 固体酸催化剂在有机反应中的应用已广受关注。但是, 传统的固体酸催化剂制备过程大多较为复杂, 获取周期长, 且酸度不均、负载量也难以实现调控, 因此有必要发展一种制备便捷、酸度适中、普适性广的固体酸催化剂。聚甲酚磺醛是2-羟基-4-甲基苯磺酸与甲醛的低聚物, 不溶于二氯甲烷、乙酸乙酯等大部分有机溶剂, 易溶于水。聚甲酚磺醛的水溶液已经被用作治疗妇科疾病的药物, 是一种廉价、易得、生物兼容性好的市售化学品。由于聚甲酚磺醛分子结构中含有大量的磺酸基, 因此其具备作为酸催化剂的潜质。考虑到其骨架结构中富含大量羟基, 可能与SiO₂类多羟基载体产生氢键作用, 因而可在一定程度上稳定制备的SiO₂/聚甲酚磺醛复合固体材料。本文采用浸渍法, 经如下两步将聚甲酚磺醛负载于SiO₂表面, 制备了一系列负载量不同(0.2~1.5 mmol/g)的复合酸性材料: (1)将SiO₂加入聚甲酚磺醛水溶液的乙醇溶液中, 在室温下磁力搅拌10~15分钟; (2)在减压条件下除去水和乙醇(约30分钟)。整个制备过程, 无需专门的设备, 仅需使用磁力搅拌器和旋转蒸发仪等一般有机合成实验室的常规仪器, 并且制备周期非常短, 在1小时以内即可完成。该方法所制备催化剂的负载量可由投料比直接控制, 可简单、快速制备负载量不同的SiO₂/聚甲酚磺醛复合固体材料。

研究发现, SiO₂/聚甲酚磺醛复合固体催化剂能够高效地促进多种有机反应, 如二苯甲醇与苯乙烯衍生物的亲核取代反应、2-苯基乙醇与醛的oxa-Pictet-Spengler反应以及吡啶与1,3-二羰基化合物或2-苯基乙醛的直接C3-烯基化反应。在上述反应中, 目标产物的产率均较高, 且反应对底物具有良好的官能团兼容性。SiO₂/聚甲酚磺醛催化剂均可重复使用多次, 且催化活性无明显下降。更重要的是, 上述反应的投料量可增加至10 mmol, 且产物的分离产率无明显下降, 从而证明SiO₂/聚甲酚磺醛催化剂具有一定的实际合成价值。值得一提的是, 由于SiO₂/聚甲酚磺醛催化剂含有一定量的水, 本文认为聚甲酚磺醛在SiO₂表面是以水溶液的形式存在, 因此在反应过程中可能是以均相催化的方式进行。

相较于传统的SiO₂负载磺酸、TiO₂负载苯磺酸以及Amberlyst-15催化剂, SiO₂/聚甲酚磺醛复合固体酸催化剂具有活性高、制备周期短、廉价易得的特点。同时, 该催化剂可简单、快速制备各种不同酸负载量的固体催化剂, 在一定范围内调控该类固体酸催化剂的酸性。因而, SiO₂/聚甲酚磺醛复合固体酸催化剂望用于各种酸催化合成反应中。

关键词: 固体酸催化剂; 聚甲酚磺醛; 酸催化; 催化剂固载化; 烷基化

收稿日期: 2015-04-25. 接受日期: 2015-05-22. 出版日期: 2015-09-20.

*通讯联系人. 电话: (027)87543032; 传真: (027)87544532; 电子信箱: klgyl@hust.edu.cn

[†]共同第一作者。

基金来源: 国家自然科学基金(21173089, 21373093); 中央高校基本科研业务费专项资金(2014ZZGH019); 湖北省催化协同创新中心资助。

本文的英文电子版由Elsevier出版社在ScienceDirect上出版(<http://www.sciencedirect.com/science/journal/18722067>).