Scientific paper

Silica Tungstic Acid as an Efficient and Reusable Catalyst for the One-pot Synthesis of 2-Amino-*4H*-chromene Derivatives

Mahnaz Farahi,* Bahador Karami, Samambar Alipour and Leila Taghavi Moghadam

Department of Chemistry, Yasouj University, Yasouj 75918-74831, Iran

** Corresponding author: E-mail: farahimb@yu.ac.ir*
Tel: +98-7412223048 Fax: +98-7412242167

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Abstract

Silica tungstic acid (STA) has been found to be an efficient and reusable solid acid catalyst for the synthesis of 2-amino-4*H*-chromenes via the three-component reaction of aromatic aldehydes, malononitrile, and β-naphthol. STA as a novel solid acid was characterized by X-ray fluorescence, X-ray diffraction, and Fourier transform infrared spectroscopy.

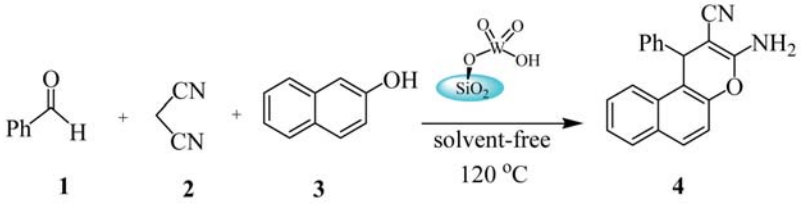
Keywords: Silica tungstic acid, heterogeneous catalyst, 2-amino-4*H*-chromenes, multi-component reactions.

1. Introduction

Recently, heterogeneous solid catalysts have been used in various organic transformations as they possess a number of advantages.[1–4] Immobilization of catalysts on solid support improves the availability of the active sites, stability of the catalyst, product separation, and catalyst recovery which are all important factors in industry.[5] Therefore, use of supported and reusable catalysts in organic transformations has economical and environmental benefits. Although supported catalysts are available on different supports including charcoal, alumina, silica, and polymers, silica has many other advantages such as lack of swelling, good mechanical and thermal stability, and ease of scalability. Silica tungstic acid (STA) as a silica supported catalyst has been used in some organic transformations.[6] This inexpensive and reusable catalyst can be readily handled and easily separated from the reaction mixture, with these advantages making reactions cleaner and faster with higher yields.

Chromene derivatives are an important class of heterocyclic compounds having significant biological activities.[7] During the last decade, these compounds have shown interesting pharmacological properties, including antimicrobial, antiviral, antioxidant, antitumor, cancer therapy, and central nervous system activities.[8–9] Many chromenes are also photoactive and can be used in various photoinduced reactions affording diverse heterocyclic compounds.[10]

One-pot multicomponent reaction (MCR) processes bringing together three or more components with high atom economy play an important role in combinatorial chemistry, so this field remains one of the most interesting areas of research in recent years. During MCRs, target compounds are produced with greater efficiency by generating structural complexity in a single step from three or more reactants.[11–13]



Scheme 1. STA-catalyzed synthesis of 2-amino-4*H*-chromenes.

Due to the advantages of MCRs and heterogeneous catalysts and in continuation of our interest in the use of heterogeneous catalysts,[6,14–17] herein we report a new methodology for the synthesis of 2-amino-4*H*-chromenes using silica tungstic acid as an efficient heterogeneous catalyst (Scheme 1).

2. Results and Discussion

Nowadays, environmental awareness has led to a search for more environmentally friendly forms of catalysis. On the other hand, development of the practical methods, reaction media, conditions and/or the use of materials based on the idea of green chemistry is one of the important issues in the scientific community. Recently, silica tungstic acid (STA) has been used as a heterogeneous solid acid in some organic syntheses.[6,18] As can be seen in Scheme 2, from the reaction of readily available materials such as silicagel and thionyl chloride, silica chloride (**5**) has been prepared. Then anhydrous sodium tungstate can react with **5** to give silica tungstic acid (**6**). This reaction is clean and easy.

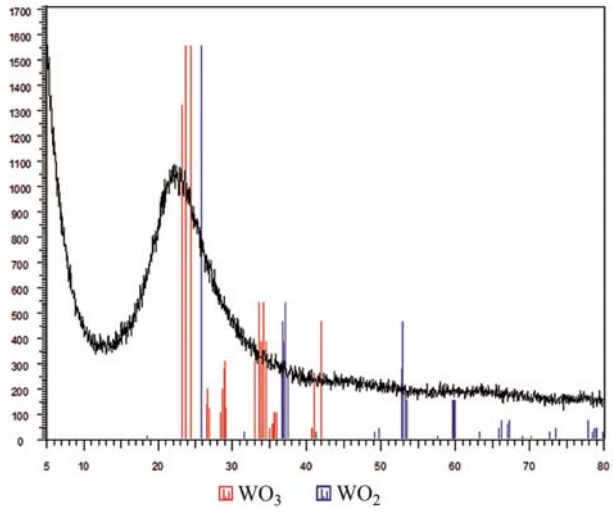
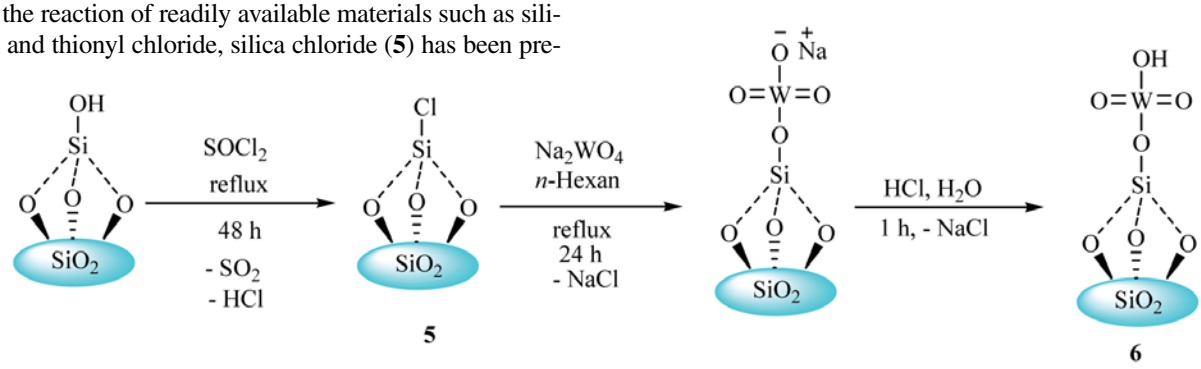


Fig. 1. The XRD of the silica tungstic acid (**6**).



Scheme 2. Preparation of silica tungstic acid (**6**).

The prepared silica tungstic acid (**6**) was characterized by X-ray fluorescence (XRF), X-ray diffraction (XRD), and FT-IR spectra. As can be seen in Table 1,

Table 1. XRF data of silica tungstic acid.

Entry	Compound	Concentration (%w/w)
1	SiO_2	81.250
2	WO_4	1.660
3	P_2O_5	0.320
4	CaO	0.023
5	SO_3	0.560
6	Fe_2O_3	0.030
7	ZnO	0.028
8	Al_2O_3	0.024
9	TiO_2	0.021
10	SrO_2	0.017
11	Y_2O_3	0.009
12	CuO	0.023
13	LOI[a]	16.29
14	Total	99.96

[a] Loss on Ignition.

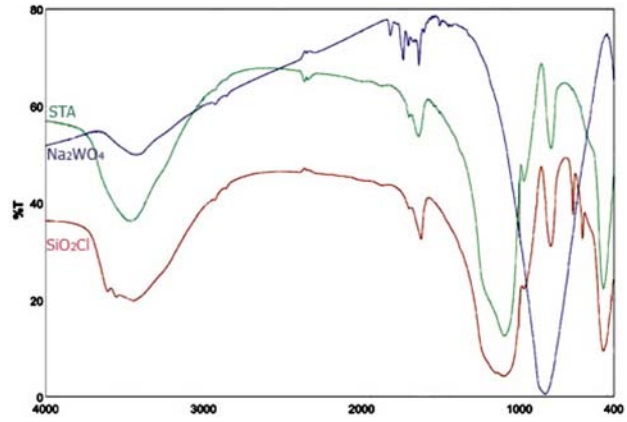


Fig. 2. FT-IR of anhydrous sodium tungstate, silica chloride (**5**), and silica tungstic acid (**6**).

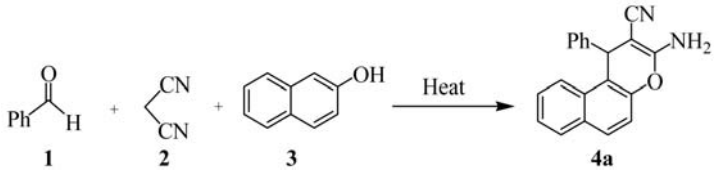
XRF data for the STA shows the composition of the catalyst as 81.25 (%w/w) SiO_2 (Entry 1) and 1.66 (%w/w) WO_4 (Entry 2).

Figure 1 depicts the XRD patterns for the silica tungstic acid (**6**) which shows the presence of tungstic acid crystalline phase supported on amorphous silica as a broad peak around 22° (2 θ) (θ is the Bragg's angle). The

three peaks in the 23–25° region of the XRD spectrum could be attributed to the presence and linking of WO_3 to the silica gel.[19]

The FT-IR spectra for the anhydrous sodium tungstate, silica chloride (**5**), and silica tungstic acid (**6**) are shown in Figure 2. These spectra show the characteristic bonds of anhydrous sodium tungstate, silica chloride (**5**), and STA. The absorption bands at 3459, 1636, 1096, 970, 1620, and 799 cm^{-1} in the catalyst spectrum reveal both bonds in SiO_2-Cl and WO_4 group. We evaluated the amounts of tungstic acid supported on SiO_2 using two methods, including (a) titration with 0.1 N NaOH (neutralization reaction) and (b) calculating the weight difference between primary solid acid loosed chloride and new silica tungstic acid. After these experiments, we found that 1 g of the catalyst includes 0.05 g OWO_3H. Regarding the molecular weight of WO_4H (249 g/mol), therefore, 1 g of the catalyst corresponds to 0.2 mmol.

Table 2. Screening conditions for the model reaction.

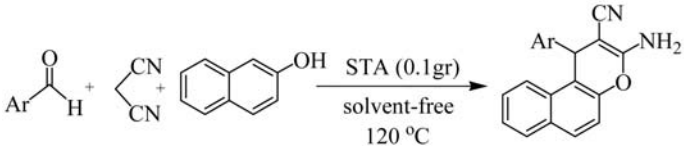


1 **2** **3** **4a**

Entry	Solvent	Catalyst loading	Temp. (°C)	Time (h)	Yield (%)[a]
1	None	None	70–80	24	10
2	None	$ZnCl_2$ (5%)	70–80	12	30
3	None	$MgBr_2$ (5%)	70–80	12	45
4	None	$ZrOCl_2$ (5%)	70–80	12	40
5	None	STA (0.5 g)	25	12	40
6	None	STA (0.5 g)	60–70	7	50
7	None	STA (0.5 g)	80–100	7	60
8	None	STA (0.5 g)	120	4	80
9	None	STA (0.2 g)	120	4	83
10	None	STA (0.1 g)	120	3	90
11	EtOH	STA (0.1 g)	70–80	5	75
12	H_2O	STA (0.1 g)	90–100	7	50
13	CH_3CN	STA (0.1 g)	70–80	5	60

[a] Isolated yields.

Table 3. STA-catalyzed synthesis of 2-amino-4*H*-chromene derivatives **4a–o**.



Entry	Ar	Product	Time (h)	Yield (%)[a]	m.p. (°C)[Lit.]
1	Ph	**4a**	3	90	273–274[25]
2	3-MeC_6H_4	**4b**	4	90	230–232[26]
3	4-MeC_6H_4	**4c**	4	85	260–263[25]
4	4-OHC_6H_4	**4d**	3	95	270–272[26]
5	2-ClC_6H_4	**4e**	3	94	231–215[27]
6	4-ClC_6H_4	**4f**	3	90	205–206[25]
7	3-CNC_6H_4	**4g**	1.5	90	238–240[26]
8	2-$NO_2C_6H_4$	**4h**	2.5	85	238–240[28]
9	3-$NO_2C_6H_4$	**4i**	2	80	232–235[25]
10	4-$NO_2C_6H_4$	**4j**	2.5	75	236–239[25]
11	2-BrC_6H_4	**4k**	3.5	86	181–183[26]
12	4-BrC_6H_4	**4l**	2	80	220–221[28]
13	3-$OMeC_6H_4$	**4m**	5	75	248–250[25]
14	4-$OMeC_6H_4$	**4n**	4	85	185–187[25]
15	3-FC_6H_4	**4o**	3	65	276–278[26]

[a] Isolated yields.

Due to the importance of novel catalyst applications, after characterization of the catalyst, we decided to use STA for the synthesis of some 2-amino-4*H*-chromene derivatives. In order to optimize the reaction conditions, a model reaction between benzaldehyde, malononitrile, and β-naphthol was carried out in the absence of the catalyst at 100–120 °C under solvent-free conditions. No chromene product was synthesized even after 24 h. Therefore the model reaction was investigated in the presence of different catalysts at various conditions (Table 2).

As illustrated in Table 2, the best result was obtained with 0.1 g STA at 120 °C under solvent-free conditions. In order to prove the versatility of this method, after optimization of the reaction conditions, different aromatic aldehydes were treated with malononitrile and β-naphthol. It was found that both electron rich and electron poor aldehydes react well in this process to afford the corresponding products **4a–o** in good to excellent yields. The obtained results are summarized in Table 3. The isolated products **4a–o** were characterized by physical and spectroscopic techniques and they were compared with authentic samples.[20–24]

The probable mechanism for the synthesis of 2-amino-4*H*-chromenes **4** in the presence of catalytic amounts of STA is outlined in Scheme 3. It seems that STA acts as a Brønsted acid so that it can releases a proton to activate the aromatic aldehyde. It can also activate malononitrile for the attack to activated the aromatic aldehyde to form intermediate **1**. Interception of intermediate **1** by β-naphthol produces an open chain intermediate **2** which upon the cyclization produces the corresponding 2-amino-4*H*-chromenes **4**.

The reusability of catalyst is an important factor for its commercial uses. Therefore, the recovery and reusability of STA was investigated. Hence, STA was successfully regenerated from the model reaction by washing with EtOH and drying at 100 °C. Using the recycled catalyst for five consecutive times in the model reaction gave the product **4a** with a gradual decreasing of the reaction yield (Figure 3).

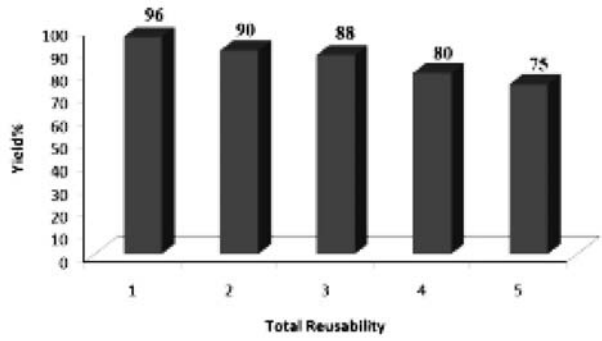
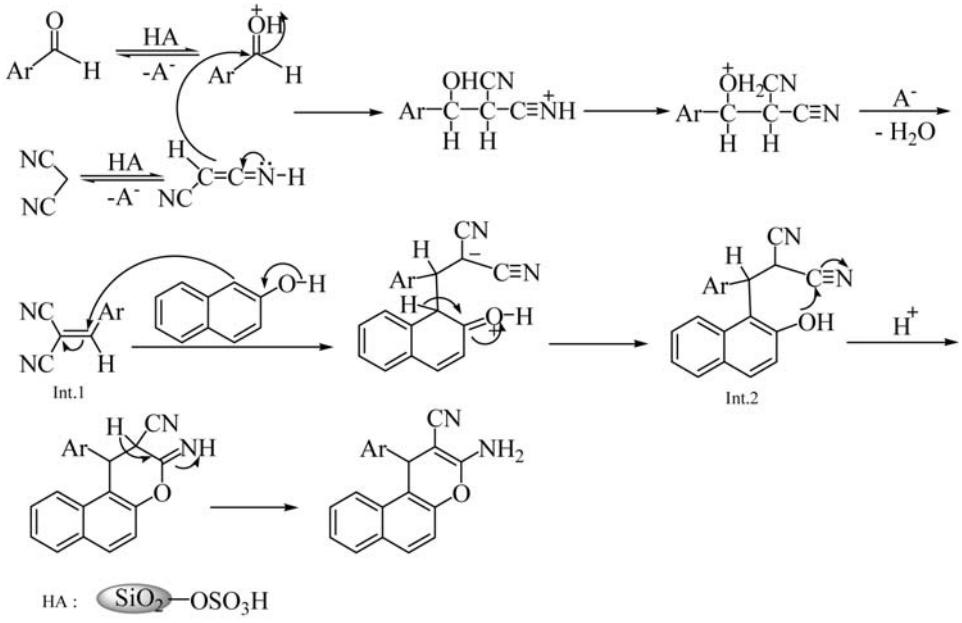


Fig. 3. Reusability study of the catalyst STA in the model reaction (synthesis of **4a**).

3. Experimental

3. 1. General

X-Ray diffraction (XRD) pattern was obtained by Philips X Pert Pro X diffractometer operated with a Ni-filtered Cu Ká radiation source. X-Ray fluorescence (XRF) spectroscopy was recorded by X-Ray Fluorescence Analyzer, Bruker, S_4 PIONEER, Germany. Chemicals were purchased from Aldrich, Fluka and Merck and used without purification. The products were isolated and identified by their spectral data. IR spectra were recorded on FT-IR JASCO-680 using KBr disks. The ^{1}H NMR and ^{13}C



Scheme 3. Proposed mechanism for STA-catalyzed synthesis of 2-amino-4*H*-chromene derivatives **4**.

NMR spectra were recorded on a Bruker instrument 400 MHz ultra shield model as $CDCl_3$ solutions.

3. 2. Preparation of Silica Chloride (5)

Silica chloride (**5**) was prepared via the previously reported procedure. Thus, thionyl chloride (40 mL) was added to an oven-dried silica-gel 60 (10 g) in a round bottomed flask (250 mL) equipped with a condenser and a drying tube and the mixture in the presence of $CaCl_2$ as a drying agent was refluxed for 48 h. The resulting white-greyish powder **5** was filtered and stored in a tightly capped bottle.[29]

3. 3. Preparation of Silica Tungstic Acid (6)

The mixture of silica chloride (**5**) (6.00 g) and sodium tungstate (7.03 g) was added to *n*-hexane (10 mL) and the resulting mixture was stirred under refluxing conditions for 4 h. After completion of the reaction, the reaction mixture was filtered, washed with distilled water, and dried and then stirred in the presence of 0.1 N HCl (40 mL) for 1 h. Finally, the mixture was filtered, washed with distilled water, and dried to afford STA.[4]

3. 4. General Procedure for the Synthesis of 2-Amino-4H-chromene Derivatives 4

To the mixture of the aromatic aldehyde (1 mmol), malononitrile (1 mmol), and β-naphthol (1 mmol) was added STA (0.1 g). The resulting mixture was stirred at 120 °C for the appropriate time (Table 3). After completion of the reaction (as indicated by TLC), the mixture was diluted with ethanol (10 mL) and the catalyst was separated by filtration. Evaporation of solvent under reduced pressure gave the product **4**. Further purification was achieved by recrystalization from $EtOH/H_2O$.

3. 5. Selected Spectral Data

3-Amino-1-(phenyl)-1*H*-benzo[*f*]chromene-2-carbonitryl (4a).[25] White solid, mp 273–274 °C. FT-IR: ν_{max} (KBr) 3410 and 3310 (NH_2), 3090, 2190 (CN), 1638 (C=C arom.), 1585, 1300, 720, 690 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ: 5.31 (s, 1H, aliph. CH), 7.00 (s, 2H, NH_2), 7.14–7.28 (m, 5H), 7.34–7.43 (m, 3H), 7.84–7.96 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 38.55, 58.36, 116.16, 117.27, 120.99, 124.11, 125.40, 127.07, 127.74, 127.55, 128.94, 129.18, 129.97, 130.64, 131.30, 146.20, 147.31, 160.18 ppm.

3-Amino-1-(*p*-tolyl)-1*H*-benzo[*f*]chromene-2-carbonitryl (4c).[25] Pale yellow solid, mp 260–263 °C. FT-IR: ν_{max} (KBr) 3410 and 3310 (NH_2), 3050, 2190 (CN), 1640 (C=C arom), 1580, 1400, 810 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ: 2.19 (s, 3H, aliph. CH), 5.26 (s, 1H), 6.99 (s, 2H. NH_2), 7.04–7.10 (m, 4H), 7.33–7.46 (m, 3H), 7.83–7.94 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 21.02, 38.22, 58.51, 116.27, 117.26, 121.06, 124.00, 125.00, 127.38, 127.50, 128.92, 129.72, 129.80, 130.66, 131.29, 136.10, 143.30, 147.24, 160.00 ppm.

3-Amino-1-(3-cyanophenyl)-1*H*-benzo[*f*]chromene-2-carbonitryl (4g).[26] Yellow solid, mp 238–240 °C. FT-IR: ν_{max} (KBr) 3400 and 3300 (NH_2), 3090, 2190 (CN), 1640 (C=C arom.), 1580, 1400, 800, 740, 690 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ: 5.48 (s, 1H, aliph. CH), 7.16 (s, 2H, NH_2), 7.37 (d, J = 9.2 Hz, 1H), 7.41–7.49 (m, 4H), 7.64–7.67 (m, 1H), 7.77 (s, 1H), 7.83 (d, J = 8 Hz, 1H), 7.92–7.98 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 37.90, 57.41, 111.94, 114.94, 117.38, 119.19, 120.72, 123.92, 125.58, 127.84, 129.07, 130.40, 130.70, 130.89, 131.14, 131.32, 132.48, 147.43, 147.69, 160.32 ppm.

3-Amino-1-(3-nitrophenyl)-1*H*-benzo[*f*]chromene-2-carbonitryl (4i).[25] Yellow solid, mp 232–235 °C. FT-IR: ν_{max} (KBr) 3400 and 3298 (NH_2), 3153, 2181 (CN), 1645 (C=C arom.), 1536, 1300, 806 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ: 5.82 (s, 1H, aliph. CH), 7.27 (s, 2H, NH_2), 7.36–7.48 (m, 4H), 7.81–8.12 (m, 6H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 39.37, 58.16, 115.56, 117.44, 118.44, 122.86, 123.93, 124.81, 125.47, 128.88, 129.06, 129.34, 129.56, 130.35, 131.66, 131.97, 132.42, 144.02, 148.21, 166.17 ppm.

3-Amino-1-(4-nitrophenyl)-1*H*-benzo[*f*]chromene-2-carbonitryl (4j).[25] Yellow solid, mp 236–239 °C. FT-IR: ν_{max} (KBr) 3450 and 3310 (NH_2), 3153, 2200 (CN), 1645 (C=C arom.), 1580, 1530, 1355, 1218, 720 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ: 5.82 (s, 1H, aliph. CH), 7.35–47 (m, 3H), 7.52 (d, J = 8.8 Hz, 3H), 7.81–7.85 (m, 4H), 8.05 (d, J = 8.4 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 41.85, 59.21, 113.42, 116.47, 17.52, 123.54, 124.05, 125.67, 127.81, 129.09, 129.79, 130.06, 131.46, 132.01, 146.78, 148.22, 152.29, 165.05 ppm.

3-Amino-1-(4-bromophenyl)-1*H*-benzo[*f*]chromene-2-carbonitryl (4l).[28] White solid, mp 220–221 °C. FT-IR: ν_{max} (KBr) 3400 and 3298 (NH_2), 3150, 2181 (CN), 1640 (C=C arom.), 1583, 1373, 1220, 837, 721, 614 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ: 5.67 (s, 1H, aliph. CH), 7.23–7.47 (m, 9H), 7.77–7.92 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 37.70, 59.03, 114.18, 117.41, 117.46, 120.54, 123.88, 125.54, 127.56, 128.92, 129.54, 130.62, 131.64, 131.77, 131.95, 144.19, 148.17, 164.40 ppm.

4. Conclusions

In summary, we have developed a simple and efficient methodology for the synthesis of 2-amino-4*H*-chromenes **4** using silica tungstic acid (STA) as a heterogene-

ous solid acid catalyst. The advantages of this work are solvent-free conditions, low catalyst loading, use of inexpensive and recyclable catalyst, and simple experimental procedure.

5. Acknowledgement

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6. References

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Povzetek

Ugotovili smo, da je silikatno volframova kislina (STA) učinkovit trdni kislinski katalizator, ki ga je mogoče uspešno reciklirati, uporaben za sintezo 2-amino-4*H*-kromenov s pomočjo trokomponentne reakcije med aromatskimi aldehidi, maloninitrilom in β-naftolom. STA predstavlja novo trdno kislino, ki je bila karakterizirana z rentgensko fluorescenčno spektroskopijo, z rentgensko difrakcijsko analizo in z infrardečo spektroskopijo s pomočjo Fourierjeve transformacije.