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Catalytic Performance of Heteropolyacids as Efficient and Eco-Friendly Catalysts for the One-Pot Synthesis of Benzopyran Derivatives

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An efficient and improved procedure for the synthesis of benzopyran derivatives has been achieved with Keggin-type and Preyssler-type heteropolyacids (HPA) catalysts in one-pot reaction under solvent-free conditions.

Keywords 1,3-hexanedione, salicylaldehyde, benzopyran derivatives, heteropolyacids, solvent-free condition

INTRODUCTION

Benzopyran and its derivatives have attracted considerable attention for organic and medicinal chemists because of their useful biological and pharmacological properties such as antibacterial, antitumor, antiallergic, anticoagulant, spasmolytic, diuretic, and potassium channel activators.[1−3] Pyrans and their derivatives are also key synthons[4] in the fields of pharmaceuticals, cosmetics, and perfumes. The biological importance of this group of compounds has evoked widespread interest in the development of new methodologies. Recently, benzopyran derivatives have been synthesized by the reaction of substituted salicylaldehydes with dimedone catalyzed by KF/Al_2O_3[5] or triethylbenzylammoium chloride (TEBA).[6] Considering the importance and wide range applications of these compounds, an easy and practical preparation method has still remained a challenging task. Development of methods using heteropolyacids (HPAs) as solid and green catalysts for fine organic synthetic processes related to fine chemicals, such as flavors, pharmaceuticals, and food industries have been under attention in the last decade.[7] HPAs were reported to be more active catalysts than conventional inorganic and organic acids for various reactions in solution.[8,9] They were used as industrial catalysts for several liquid-phase reactions such as esterification, etherification, hydration and dehydration, de-esterification, and condensation reactions.[10]

In continuation of our interest in the application of heteropolyacids as versatile catalysts for a variety of organic transformations,[11−17] we would like to report an effective method to produce benzopyran derivatives in high yields, catalyzed by Preyssler type and Keggin type heteropolyacids, under solvent-free conditions (Scheme 1). Our findings indicated that both HPA catalysts are effective for the synthesis of these compounds in high yields. The major aim described in this work is to design and develop the applications of HPAs with their exclusive properties.

EXPERIMENTAL

Materials and Methods

Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus. ^{1}HNMR spectra were recorded on a Bruker AQS AVANCE-300MHz spectrometer using TMS as an internal standard ($CDCl_3$ solution). IR spectra were recorded using KBr disk on the FT-IR Bruker Tensor 27. All products were well characterized by comparison with authentic samples by TLC, spectral, and physical data.

General Procedure

A mixture of substituted salicylaldehyde (2 mmol, 0.24 g), substituted 1, 3-hexanedione (4 mmol, 0.56 g), and heteropolyacid (0.03 mmol) were mixed and stirred for 20 min at room temperature. Temperature was raised to 120°C and maintained for the specified time (Table 3). After completion of the reaction (monitored by thin-layer chromatography, TLC), the reaction mixture was diluted with water (10 mL) and stirred for 5 min at

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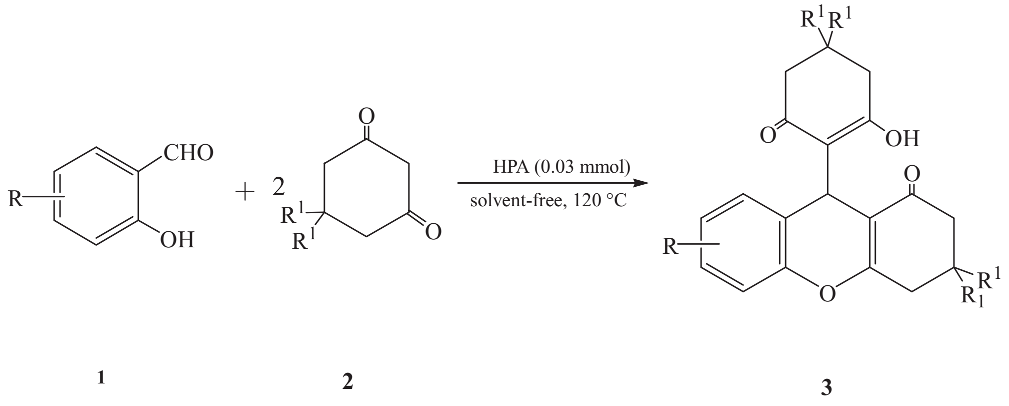


SCH. 1. Synthesis of benzopyran derivatives catalyzed by $H_{14}[NaP_5W_{29}MoO_{110}]$ heteropolyacid, under solvent-free conditions.

80°C. The product was filtered and purified by recrystallization from ethanol.

RESULTS AND DISCUSSION

To obtain some preliminary information on this synthetic reaction, initial experiments were performed with salicylaldehyde (1) and 5, 5- dimethyl-1, 3-cyclohexanedione (2, R^1 =Me) as model substrates. When salicylaldehyde (2 mmol) was treated with 5, 5- dimethyl-1, 3-cyclohexanedione (4 mmol) in the presence of a catalytic amount of HPA (0.03 mmol) at 120°C, the desired product (3a) was obtained in 95% yield. In continuation of our works, using heteropolyacids, which are low in toxicity, being highly stable towards humidity, being recyclable, air stable, and very well known in green chemistry, we studied this reaction with heteropolyacids including Mo, such as $H_3[PMo_{12}O_{40}]$, $H_4[PMo_{11}VO_{40}]$, $H_5[PMo_{10}V_2O_{40}]$, $H_6[PMo_9V_3O_{40}]$ and $H_{14}[NaP_5W_{29}MoO_{110}]$. Mixed addenda Preyssler and Keggin catalysts are formed by the substitution of tungsten (VI) ion by Mo (VI). Interestingly, these catalysts, not only catalyzed this reaction, but also showed higher yields than $H_3[PW_{12}O_{40}]$ and $H_{14}[NaP_5W_{30}O_{110}]$, which were used in our earlier work.[17]

The effects of various parameters such as solvent, catalyst type, time, and temperature of reactions were studied. The effect of solvent was studied by carrying out the reactions in various solvents including ethanol, water, and acetonitrile, and solvent-free condition. As presented in Table 1, the solvent free condition resulted in higher yields.

In study of reaction progress with TLC, we found that conversion rates were affected by catalyst structure. In all cases the conversion rates were higher with $H_{14}[NaP_5W_{29}MoO_{110}]$. This result is in agreement with expectation and earlier works on Biginelli reaction.[12,13] In this work, Preyssler-type heteropolyacid gives higher yields of products than Keggin-type heteropolyacids. Unlike the Keggin-type heteropolyacids that have been widely used as acid and oxidation catalysts for organic syntheses, the role of Preyssler catalyst is largely overlooked and there is not sufficient information. We believe that the Preyssler-type form activates the pseudo liquid phases by maintaining the concentration of reactant molecules in the appropriate pseudo liquid (solid bulk) phase, and this is due to the "oval" shape of the Preyssler-type in contrast to the "spherical" Keggin-type polyanions, which tend to be absorbing a greater number of reactant molecules.[18] The order of efficiency of these catalysts is as follows: $H_{14}[NaP_5W_{29}MoO_{110}] > H_6[PMo_9V_3O_{40}] > H_5[PMo_{10}V_2O_{40}] > H_4[PMo_{11}VO_{40}] > H_3[PMo_{12}O_{40}]$. Thus, $H_{14}[NaP_5W_{29}MoO_{110}]$ was selected as the catalyst of choice for the synthesis of benzopyran. The results are represented in Table 2.

TABLE 1
The results of the reaction of salicylaldehyde (1) and 5, 5-dimethyl-1, 3-cyclohexanedione (2) in the presence of $H_{14}[NaP_5W_{29}MoO_{110}]$ in different solvents

Entry	Solvent	Temperature (°C)	Time (min)	Yield (%)
1	EtOH	reflux	60	80
2	H_2O	reflux	20	80
3	CH_3CN	reflux	60	85
4	Solvent- free	120	20	95

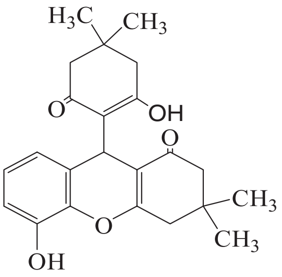
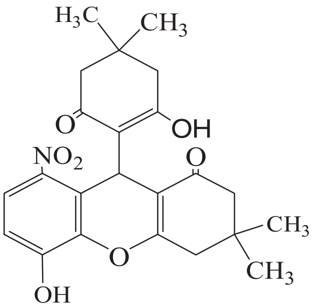
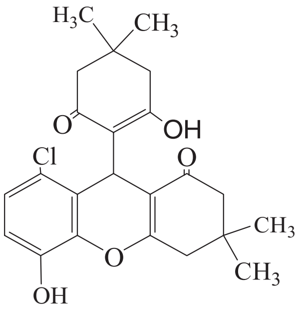
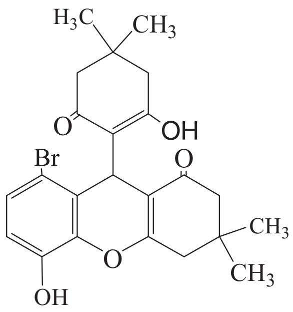
TABLE 2
The results of the reaction of salicylaldehyde (1) and 5, 5-dimethyl-1, 3-cyclohexanedione (2) using different heteropolyacids (0.03 mmol) under solvent-free conditions

Entry	Heteropolyacid	Time (min)	Yield (%)^a
1	$H_3[PMo_{12}O_{40}]$	60	70
2	$H_4[PMo_{11}VO_{40}]$	60	70
3	$H_5[PMo_{10}V_2O_{40}]$	60	80
4	$H_6[PMo_9V_3O_{40}]$	60	85
5	$H_{14}[NaP_5W_{29}MoO_{110}]$	20	95

The corresponding products were obtained in good to excellent yields. The results are summarized in Table 3.

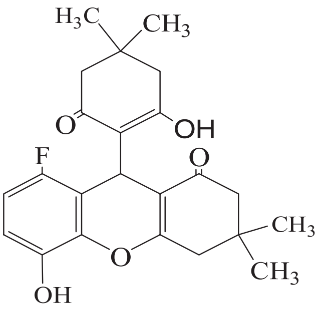
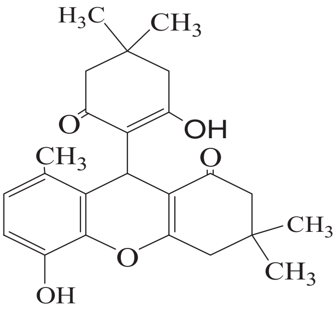
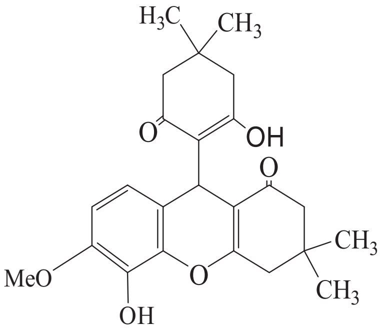
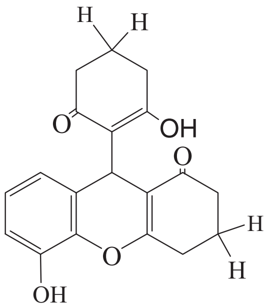
In order to obtain the best reaction temperature, the effect of reaction temperature on the yield of products was studied. The results (in optimum conditions) for $H_{14}[NaP_5W_{29}MoO_{110}]$ (best catalyst) are shown in Figure 1. The results indicated that there is an increase in the percentage of produced benzopyran with increase in the reaction temperature

TABLE 3
Synthesis of 1-oxo-hexahydroxanthene derivatives catalyzed by $H_{14}[NaP_5W_{29}MoO_{110}]$

						Mp (°C)	
Entry	Aldehydes	Products	R_1	Time (min)	Yield (%)^a	Found	(Lit)
3a	2–OHC_6H_4CHO		CH_3	20	95	209–211	206–208[4]
3b	2–OH–5–$NO_2C_6H_4CHO$		CH_3	18	90	205–208	205–207[4]
3c	2–OH–5–ClC_6H_4CHO		CH_3	25	85	238–239	238–239[4]
3d	2–OH–5–BrC_6H_4CHO		CH_3	20	90	251–253	253–255[4]

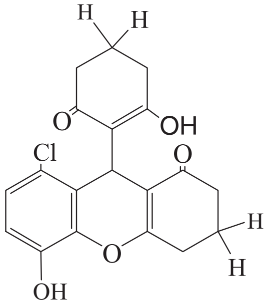
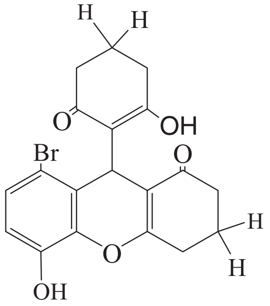
(Continued on next page)

TABLE 3
Synthesis of 1-oxo-hexahydroxanthene derivatives catalyzed by $H_{14}[NaP_5W_{29}MoO_{110}]$ *(Continued)*

						Mp (°C)	
Entry	Aldehydes	Products	R_1	Time (min)	Yield (%)[a]	Found	(Lit)
3e	2–OH–5–FC_6H_4CHO		CH_3	20	92	227–230	225–227[19]
3f	2–OH–5–MeC_6H_4CHO		CH_3	30	90	226–228	222–224[5]
3g	2–OH–3–$MeOC_6H_4CHO$		CH_3	25	85	230–232	230–231[19]
3h	2–OHC_6H_4CHO		H	25	90	244–247	245–247[4]

(Continued on next page)

TABLE 3
Synthesis of 1-oxo-hexahydroxanthene derivatives catalyzed by $H_{14}[NaP_5W_{29}MoO_{110}]$ *(Continued)*

Entry	Aldehydes	Products	R_1	Time (min)	Yield (%)^a	Mp (°C)	
						Found	(Lit)
3i	2–OH–5–ClC_6H_4CHO		H	40	85	245–247	245–247[4]
3j	2–OH–5–BrC_6H_4CHO		H	35	88	236–240	235–236[4]

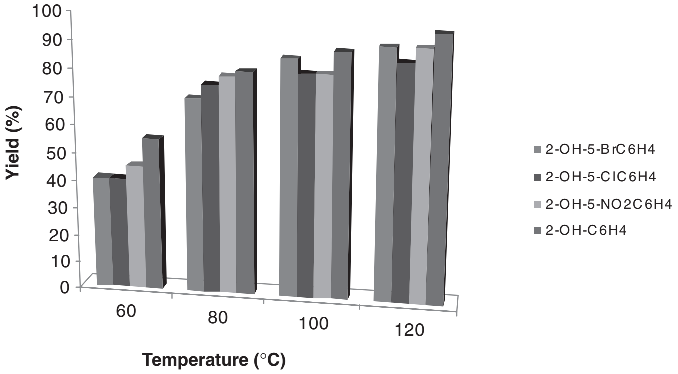


FIG. 1. Effect of the reaction temperature on products yield of salicylaldehyde (1) and 5, 5-dimethyl-1, 3-cyclohexanedione derivatives in the reactions catalyzed by $H_{14}[NaP_5W_{29}MoO_{110}]$.

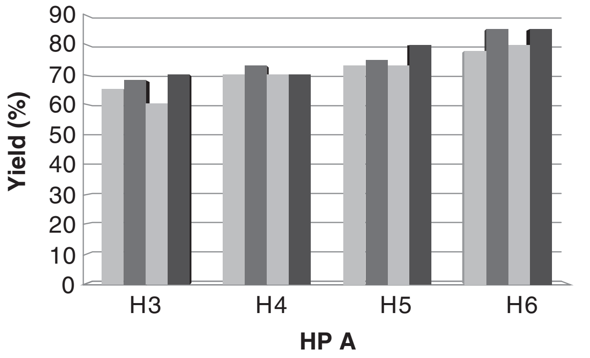


FIG. 2. Comparison catalytic performance of keggin heteropolyacids on products' yield.

up to 120°C. This behavior was generally quiet for all of the used catalysts. The optimum reaction temperature has been found to be 120°C under solvent-free conditions.

Comparison of $H_6[PMo_9V_3O_{40}]$, $H_5[PMo_{10}V_2O_{40}]$, $H_4[PMo_{11}VO_{40}]$, and $H_3[PMo_{12}O_{40}]$ showed that the higher activity could be achieved with $H_6[PMo_9V_3O_{40}]$. The results are represented in Figure 2.

CONCLUSION

Preyssler-type heteropolyacid $H_{14}[NaP_5W_{29}MoO_{110}]$ is a highly efficient solid acid catalyst for the synthesis of benzopyran derivatives under solvent-free conditions. The short reaction times, simple work-up in isolation of the products in high yields with high purity, mild reaction conditions, and reusability of catalyst are some advantages of this protocol.

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