



ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2019, 11(1): 71-74
(<http://www.derpharmachemica.com/archive.html>)

Calcined Tungstophosphoric Acid: An Efficient Catalyst for One-pot Three-component Betti Bases Synthesis at Mild Reaction Condition

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ABSTRACT

An efficient one-pot three-component Betti bases synthesis procedure has been developed. In the current study, substituted aldehydes β -naphthol and aniline have been used in the presence of calcined tungstophosphoric acid as a heterogeneous catalyst with dichloromethane as a solvent at room temperature. Calcined (X) form of tungstophosphoric acid was compared with non calcined (Y) in terms of product yield and reaction time. The former exhibited better performance as compared to the latter. The study concluded that calcined tungstophosphoric acid acts as an efficient environmentally friendly catalyst for the one-pot three-component Betti bases synthesis under mild condition.

Keywords: Tungstophosphoric acid, Betti bases, Calcination, Catalyst.

INTRODUCTION

Betti reaction is one of the important multicomponent syntheses which were developed in the early twentieth century by Mario Betti [1]. The reaction is characteristically an amino alkylation reaction with carbon-carbon and carbon-nitrogen bond formation simultaneously [2]. A typical Betti reaction is a modified Mannich reaction, where 2-naphthol, benzaldehyde and amine derivatives react together to provide 1-(α -aminoalkyl)-2-naphthols, commonly called Betti bases [3]. Recently, more attention has been given to Betti bases as seen in numerous biological [4,5], catalytic [6,7] and synthetic applications [8,9].

Classical Betti bases were initially prepared by reacting ammonia or urea, an aldehyde and β -naphthol in alcoholic potassium hydroxide solution in two steps taking several hours (9-36 h) [9]. Later, one-pot three component methods were adopted to overcome the demerits of the classical method by selecting different reacting species [10-13]. Unfortunately, such methods also suffered from shortcomings including side reactions, long reaction time and low yields.

Recently, several green and convenient techniques have been also developed to synthesize Betti bases [14,15]. These were also reported in the preparation of 1-amidoalkyl-2-naphthol by the condensation of aryl aldehydes, β -naphthol and acetonitrile or amide in the presence of Bronsted or Lewis acid catalysts such as Ce (SO₄)₂ [16], K₅CoW₁₂O₄₀.3H₂O [17] and SiO₂-FeCl₃ [18].

Tungstophosphoric acid (H₃PW₁₂O₄₀), a class of heteropoly acid (HPA), having Bronsted acid properties has recently gained recognition in organic synthesis [19,20]. Tungstophosphoric acid has high thermal stability and high solubility in polar solvents [21]. It was also reported that tungstophosphoric acid proved to be stronger than common mineral acids (HCl, H₂SO₄, HNO₃) and upon calcination (up to 400°C) develop super acid sites [22,23].

In the present investigation, synthesis of Betti bases has been reported by using calcined tungstophosphoric acid as a catalyst. Further, both the physical forms (calcined, non-calcined) of tungstophosphoric acid performance were evaluated in terms of yield, time of reaction and amount of catalysts.

MATERIALS AND METHODS

All the materials and chemicals were procured from Sigma Aldrich. Fourier Transform Infrared (FTIR) spectra for the synthesized compounds were taken by thermo scientific iD5 ATR diamond Nicolet iS 5FTIR spectrometer. Proton Nuclear Magnetic Resonance (¹H-NMR) and Carbon-13 Nuclear Magnetic Resonance (¹³C-NMR) spectra of compounds were recorded with BRUKER-PLUS (400 MHz). Calcination of catalyst (tungstophosphoric acid) was performed using thermocraft incorporated tube furnace.

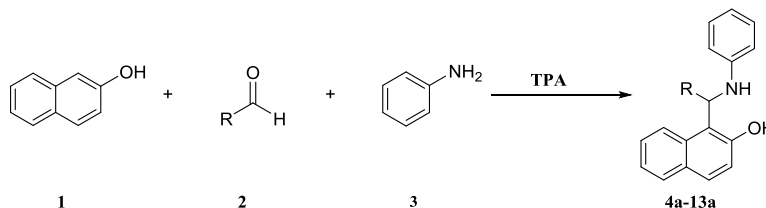
Tungstophosphoric acid calcination

An accurately weighed tungstophosphoric acid was taken in crucible and placed in a tube furnace around 400°C up to 4 h.

General procedure for the synthesis of betti bases (4a-13a) via one-pot multicomponent reaction using tungstophosphoric acid

A mixture of aldehydes (2 mmol), β -naphthol (2 mmol) and aniline (2.5 mmol) was stirred in dichloromethane (DCM) in presence of varying mol% of calcined as well as non-calcined tungstophosphoric acid at room temperature. The resulting product was obtained by recrystallization of ethanol.

A general Scheme 1 for the Betti bases is shown in the figure below.



Scheme 1: A schematic representation of the formation of Betti bases (4a-13a) from β -naphthol (1), aldehydes (2) and Aniline(3)

Spectral data of few selected compounds

1-((phenylamino)(2,4,6-trimethoxyphenyl)methyl)naphthalene-2-ol (5a)

FTIR (cm^{-1} , ATR); 3388 (NH), 3200 (OH), 1602 (C=C, Ar); $^1\text{H-NMR}$ (DMSO) δ (ppm)=10.2 (1H, s, OH), 8.93 (1H, s, Ar-H), 7.07-7.77 (9H, m, Ar-H), 6.50 (1H, br, NH), 5.76 (1H, s, CH), 3.45-3.82 (9H, s, OCH_3); $^{13}\text{C-NMR}$ (DMSO) δ (ppm)=172.33, 165.60, 156.82, 130.12, 130.04, 129.47, 123.09, 122.43, 100.78, 92.47, 57.88, 57.48.

1-(indolin-2-yl)(phenylamino) methyl)naphthalene-2-ol (6a)

FTIR (cm^{-1} , ATR); 3371 (NH), 3220 (OH), 1622 (C=C, Ar); $^1\text{H-NMR}$ (DMSO) δ (ppm)=9.93 (1H, s, NH, indole), 9.39 (1H, s, OH), 8.29 (1H, d, Ar-H, $J=10.2$ Hz), 8.10-8.08 (1H, d, CH, $J=7.6$ Hz), 8.80 (1H, s, NH), 7.17-7.75 (16H, m, Ar-H); $^{13}\text{C-NMR}$ (DMSO) δ (ppm)=168.41, 163.65, 155.80, 130.16, 130.08, 129.44, 124.01, 124.33, 100.98, 91.50, 56.40, 54.22.

1-((phenylamino)(1H-pyrrol-2-yl)methyl) naphthalen-2-ol (7a)

FTIR (cm^{-1} , ATR); 3346 (NH), 3204 (OH), 1621 (C=C, Ar); $^1\text{H-NMR}$ (DMSO) δ (ppm)=11.76 (1H, s, NH, pyrrole) 10.21 (1H, s, OH), 9.71 (1H, s, Ar-H), 9.48 (1H, br, NH), 6.98-7.77 (10H, m, Ar-H), 6.21-6.71 (3H, m, pyrrole) 5.01 (1H, s, CH); $^{13}\text{C-NMR}$ (DMSO) δ (ppm)=155.73, 152.62, 150.99, 149.06, 135.05, 131.04, 129.75, 129.65, 129.26, 128.18, 127.99, 126.56, 126.44, 126.37, 124.30, 123.09, 121.20, 119.06, 116.90, 116.08, 114.32, 110.16, 109.09.

1-(1-(phenylamino)pentyl)naphthalen-2-ol (12a)

FTIR (cm^{-1} , ATR); 3392 (NH), 3208 (OH), 1598 (C=C, Ar); $^1\text{H-NMR}$ (DMSO) δ (ppm)=8.79(1H, br, NH), 7.17-8.20 (10H, m, Ar-H), 3.12-3.10 (1H, d, CH, $J=7.6$ Hz), 2.95-2.93(2H, t, CH_2 , $J=8.4$ Hz), 1.81-1.77(2H, t, CH_2 , $J=14.8$ Hz), 0.85(1H, s, CH_3); $^{13}\text{C-NMR}$ (DMSO) δ (ppm)=155.26, 145.49, 137.03, 128.58, 122.57, 121.89, 119.53, 60.22, 22.72, 19.02, 14.56.

RESULTS AND DISCUSSION

Typical Betti bases (4a-13a) were synthesized from β -naphthol, aldehydes and aniline under the influence of tungstophosphoric acid catalyst. Calcined form of tungstophosphoric acid was used to compare the product under optimized reaction conditions.

Compound 5a, synthesized from β -naphthol, 2,4,6-trimethoxy benzaldehyde and aniline was considered as a model compound to assess the effect of calcined (X) as well as non-calcined (Y) tungstophosphoric acid in dichloromethane as a solvent at room temperature (Table 1).

Table 1: Effect of calcined (X), non-calcined (Y) tungstophosphoric acid and other catalysts for the synthesis of model Betti base (5a)

Entry ¹	Catalyst (mol%)	Yield ² (%)	Solvents (ml)	Time	Temperature (°C)	References
1	X (4)	69	DCM(8)	60 min	RT	-
2	X (6)	75	DCM(8)	50 min	RT	-
3	X (8)	84	DCM(8)	35 min	RT	-
4	X (10)	100	DCM(8)	10 min	RT	-
5	X (15)	92	DCM(8)	15 min	RT	-
6	Y (4)	53	DCM(8)	100 min	RT	-
7	Y(6)	58	DCM(8)	80 min	RT	-
8	Y(8)	71	DCM(8)	65 min	RT	-
9	Y(10)	84	DCM(8)	45 min	RT	-
10	Y(15)	79	DCM(8)	40 min	RT	-
11	NBS (10)	56	Ethanol-Water (-)	60 min	60	[24]

12	Ce(SO ₄) ₂ (-)	72	Acetonitrile	72 h	85	[16]
13	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (1.5)	90	1,2-dichloroethane	4 h	125	[25]
14	<i>p</i> -TSA	93	1,2-dichloroethane	12 h	RT	[26]

¹Reaction conditions were optimized to 100% conversion; ²Isolated yields

The yield of Betti base percentage was increased as the mol% of both forms of tungstophosphoric acid was increased. With each mol% of catalyst, increment % yield of product and time of reaction was clearly examined. Using 10% of a calcined version of tungstophosphoric acid (X), a maximum yield of 100% in 10 min of time was obtained while only 84% yield was obtained at same mol% with the expense of 45 min (Table 1, entries 4, 9). When the amount of catalyst (X or Y) was increased to 15%, there was no further increase in yield (entries 5, 10). Therefore, it can be claimed that 10 mol% of the two physical forms of tungstophosphoric acid is optimum amount for such reaction. Further, the amount and physical nature of catalysts have a great impact on the yield and time of completion of each Betti base. Variation in the results indicated that the calcined form (X) of tungstophosphoric acid is more effective than non calcined form (Y) in relation to product formation. It was further postulated that upon calcination catalytic activity of tungstophosphoric acid was increased due to enhancement in Bronsted acid activity [22,23]. The results of few selected catalysts (NBS, Ce(SO₄)₂, K₅CoW₁₂O₄₀·3H₂O, *p*-TSA) were also compared and tested using in a different solvent system and different temperature condition (Table 1, entries 11,12,13,14).

In order to develop the scope of multicomponent reaction, different types of aromatic, aliphatic and heterocyclic aldehydes were reacted with β -naphthol, and aniline under the influence of both forms of the tungstophosphoric acid (X, Y) (Table 2 and Figure 1).

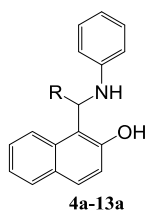


Figure 1: Structure of Betti bases (4a-13a)

Table 2: Calcined (X) and non calcined (Y) tungstophosphoric acid (10% mol) catalyzed Betti bases synthesis from β -naphthol, aldehydes and aniline

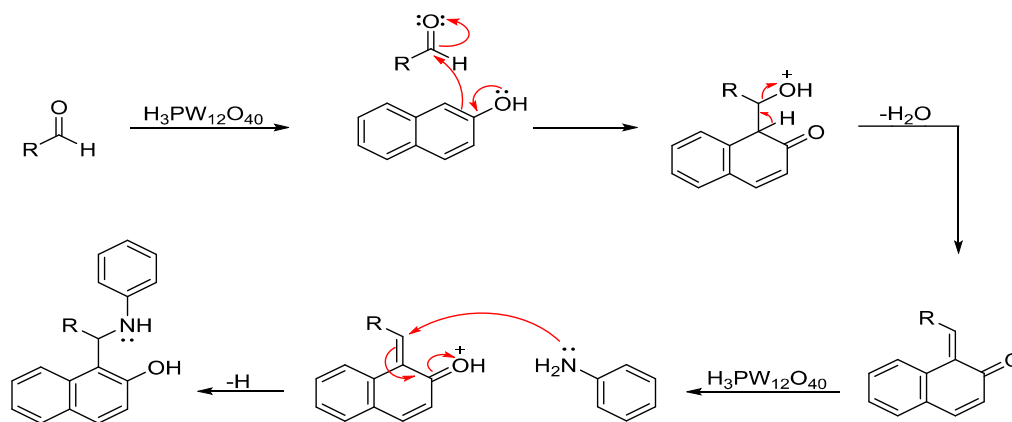
Entry	R	Product	Time (min)		Yield (%)	
			X	Y	X	Y
1		4a	10	50	92	79
2		5a	10	45	100	84
3		6a	20	60	90	80
4		7a	15	55	88	78
5		8a	10	45	90	82
6		9a	15	50	81	75
7		10a	25	60	83	70
8		11a	20	50	75	65
9		12a	22	60	85	76
10		13a	15	48	96	89

The Betti bases having aromatic and heterocyclic aldehydic partner exhibited higher yields in a short time with regard to aliphatic aldehydes in presence of calcined (X) as well as non calcined tungstophosphoric acid. These differences in the results might be due to the influence of steric hindrance of hydrocarbon chain linked with aldehydic functional group.

Plausible mechanism

It has been investigated that the reaction between aldehydes and β -naphthol in the presence of acid catalyst produced an intermediate known as ortho quinone methides, which was further reacted with aniline to form 1-amidoalkyl-2-naphthol derivatives (Betti bases) [27]. Briefly, the mechanism can be explained by assuming the nucleophilic addition of aniline to the α , β -carbonyl group compound, obtained as a result of ortho quinone methides intermediate. Afterward, the addition of aniline leads to rearrangement and aromatization affording final Betti base.

A possible mechanism for the synthesis of Betti bases (4a-13a) catalyzed by tungstophosphoric acid is shown below in Scheme 2.



Scheme 2: The plausible mechanism involved for Betti bases synthesis via one pot three-component reaction using tungstophosphoric acid as catalyst

CONCLUSION

In conclusion, in the current work, an easy technique has been reported to synthesize one-pot three-component reaction for Betti bases synthesis using calcined tungstophosphoric acid in dichloromethane as a solvent simply at room temperature. The calcined version of tungstophosphoric acid was found more effective for the product formation in the limited time of frame with high yield. Moreover, heat treated tungstophosphoric acid can be used for different condensation reactions.

ACKNOWLEDGEMENT

I am very grateful to Prince Sattam Bin Abdulaziz University for providing facilities for successful completion of this research work.

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