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Polyvinylpolypyrrolidone supported antimony(III) chloride (PVPP-$SbCl_3$): An efficient catalyst for the synthesis of chromenylphenylpropanones

Vahid Nabatchi Ahmadi, Masoud Mokhtary*

Department of Chemistry, Rasht Branch, Islamic Azad University, Rasht, Iran.

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ABSTRACT

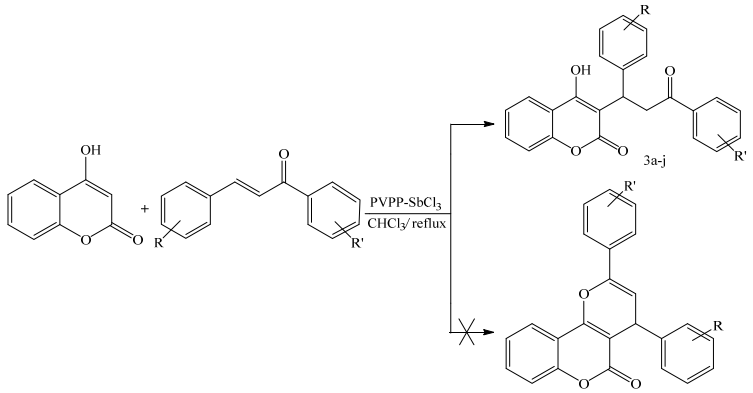
An efficient synthesis of chromenylphenylpropanone derivatives as warfarine-like analogues was developed by the Michael addition of 4-hydroxycoumarin to *α,β*-unsaturated compounds in the presence of polyvinylpolypyrrolidone supported antimony(III) chloride (PVPP-$SbCl_3$) as a new polymeric Lewis acid catalyst in chloroform at reflux conditions without formation of 2,4-diarylpyrano[3,2-*c*]chromen-5(4*H*)-ones. The synthesized compounds were identified by FT-IR, ^{1}HNMR and ^{13}CNMR spectroscopic techniques and elemental analysis. Polyvinylpolypyrrolidone supported antimony(III) chloride was characterized via Fourier transform infrared spectroscopy (FT-IR), thermal gravimetric analysis (TGA), scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy (EDX). Clean methodologies, simple preparation of the catalyst, good yields, environmentally friendly and reusable catalyst are some advantages of this work.

Keywords: *Polyvinylpolypyrrolidone, Chromenylphenylpropanones, α,β-Unsaturated compounds, 4-Hydroxycoumarin, Antimony trichloride.*

1. Introduction

Coumarin derivatives constitute an important class of compounds with a wide range of biological properties [1,2] and in particular, they are important as photochemotherapeutic agents that are used to treat a variety of skin diseases [3]. Also, they have been found to exhibit antitumor, antioxidant [4] and anti-inflammatory [5] activities. Some phenyl coumarins and chalcones have been proposed as suppressors of LTR dependent transcription, but the mechanism of action has not been fully characterized [6]. Recent research suggests that the connection of a chalcone moiety with the coumarin ring appears quite promising for the synthesis of derivatives with enhanced TPA cross-sections [7]. The conventional synthesis of pyrano[3,2-*c*]coumarins involves 1,4-conjugate addition of 4-hydroxycoumarin to chalcones [8-11]. Antimony (III) chloride has attracted attention due to its availability as a cheap commercial reagent and it was reported to catalyze different organic transformations such as conversion of epoxides into *β*-hydroperoxy alcohols [12], synthesis of 9-aryl-3,4,5,6,7,9-hexahydro xanthene-1,8-diones [13], pyrano- and furanoquinoline derivatives [14,15], dihydropyrimidinones [16], bis(indolyl)methanes [17], Michael addition of indoles to *α,β*-unsaturated ketones [18], Biginelli reaction [19] and chemoselective ring opening of oxiranes [20]. There are a number of advantages of using polymer immobilized catalysts since the reactions can be performed under mild conditions, and separation of the product is simplified. Polymer immobilized catalysts can also be recycled after use [21]. In connection of our interest in using polyvinylpolypyrrolidone as an insoluble solid support for preparation of new polymeric catalyst in some organic reactions [22-25], herein, an efficient synthesis of chromenylphenylpropanones as a warfarine-like analogues has been developed by the Michael addition of 4-hydroxycoumarin to *α,β*-unsaturated compounds in the presence of polyvinylpolypyrrolidone supported antimony(III) chloride as a new polymeric catalyst in chloroform at reflux conditions without formation of 2,4-diarylpyrano [3,2-*c*]chromen-5(4*H*)-ones (Scheme 1).

*Corresponding author email: mmokhtary@iaurasht.ac.ir
Tel.: +98 13 3342 4087; Fax: +98 13 3342 3621



3a: R = H, R′ = H **3b**: R = H, R′ = 4-Cl **3c**: R = 4-Cl, R′ = H **3d**: R = 4-Br, R′ = H **3e**: R = H, R′ = 4-MeO

3f: R = 3-NO_2, R′ = H **3g**: R = 4-Cl, R′ = 4-Cl **3h**: R = 4-MeO, R′ = H **3i**: R = 4-F, R′ = 4-Cl **3j**: R = 4-$(Me)_2N$, R′ = 4-Cl

Scheme 1. Synthesis of chromenylphenylpropanones catalyzed by PVPP-$SbCl_3$.

2. **Experimental**

2.1. General

High-purity chemical reagents were purchased from the Merck Chemical Company. Melting points were determined using an Electrothermal Mk3 apparatus and were uncorrected. NMR spectra were recorded in DMSO-d_6 on a Bruker Avance DRX-400 MHz instrument spectrometer using TMS as internal standard. Fourier transform infrared (FT-IR) spectra were performed in the transmission mode (Shimadzu, SP-1100, P-UV-Com instrument) on powder samples which were ground with KBr and compressed into a pellet. The thermal stability was determined by thermogravimetric analysis (TGA, Mettler Toledo). The TGA thermogram was recorded at a heating rate of 10 °C/min in the temperature ranging from room temperature to 600 °C in an inert atmosphere. Scanning Electron Microscopy (SEM) analysis was performed in order to investigate the microstructure of the sample using digital scanning microscope VEGA model.

2.2. Preparation of the catalyst

To a suspension of PVPP (1 g) in CH_2Cl_2 (25 mL), a solution of antimony(III) chloride (0.97 g, 4.25 mmol) in CH_2Cl_2 (15 mL) was added dropwise and the mixture stirred for 2 h at room temperature. The resulting resin was filtered and washed with CH_2Cl_2 (2×10 mL) and dried in a vacuum desiccator to give PVPP-$SbCl_3$ as a white stable powder.

2.3. General method for the synthesis of chromenylphenylpropanones

To a solution of 4-hydroxycoumarin (0.162 g, 1.0 mmol) and chalcones (1 mmol) in $CHCl_3$ (5 ml), polyvinylpolypyrrolidone-$SbCl_3$ (0.05 g) was added. The reaction mixture was heated in an oil bath to reflux for the time indicated in Tables 1 (monitored by TLC). After completion of the reaction, the solvent was removed in vacuo and the crude residue was subjected to column chromatography (EtOAc: n-hexane 1:4) to afford the desired product.

Spectral data of the new compounds

*4-Hydroxy-3-(1-(3-nitrophenyl)-3-oxo-3-phenylpropyl)-2H-chromen-2-one (**3f**):*

White solid. m.p.= 187-189 °C. FT-IR (KBr): $\bar{\nu}$= 757, 1080, 1348, 1490, 1529, 1568, 1618, 1693, 2852, 2920, 3400 cm^{-1}. ^{1}HNMR (400 MHz, $CDCl_3$): δ= 3.83 (dd, *J* = 19.1, 1.6 Hz, 1H), 4.52 (dd, *J* = 19.1, 10.4 Hz, 1H), 5.03 (dd, *J* = 10.4, 1.6 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 1H), 7.32-7.36 (m, 1H), 7.45-7.50 (m, 1H), 7.52-7.57 (m, 3H), 7.76-7.70 (m, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 8.09 (d, *J* = 1.2 Hz, 1H), 8.11-8.35 (m, 4H), 10.17 (s, 1H) ppm. ^{13}CNMR (100 MHz, $CDCl_3$): δ= 36.5, 39.9, 107.1, 116.4, 116.8, 121.9, 122.8, 123.3, 124.1, 125.1, 128.8, 128.9, 129.4, 133.8, 134.2, 135.4, 141.5, 148.1, 152.9, 161.8, 162.7, 202.1 ppm. Anal. Calcd. (%) for $C_{24}H_{17}NO_6$: C, 69.39; H, 4.12, N, 3.37. Found: C, 69.51; H, 4.06, N, 3.41.

*3-(3-(4-chlorophenyl)-1-(4-fluorophenyl)-3-oxopropyl)-4-hydroxy-2H-chromen-2-one (**3i**):*

White solid. m.p.= 184-186 °C. FT-IR (KBr): $\bar{\nu}$= 757, 827, 1095, 1224, 1386, 1506, 1566, 1616, 1683, 2852, 2923, 3417 cm^{-1}. ^{1}HNMR (400 MHz, $CDCl_3$): δ = 3.71 (d, *J* = 18.0 Hz, 1H), 4.44 (dd, *J* = 19.2, 10.4 Hz, 1H), 4.91 (d, *J* = 9.6 Hz, 1H), 7.01 (t, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.28-7.55 (m, 6H), 8.00-8.05 (m, 3H), 9.80 (s, 1H) ppm. ^{13}CNMR (100 MHz, $CDCl_3$): δ= 34.5, 40.3, 107.8, 114.9 (d, $^2J_{CF}$ = 21 Hz), 116.3, 123.9, 124.0, 128.9, 129.2, 129.7 (d, $^3J_{CF}$ = 7 Hz), 130.0, 131.9, 133.9, 135.5, 141.2, 152.9, 160.3 (d, $^1J_{CF}$ = 243

Hz), 161.1, 162.0, 201.2 ppm. Anal. Calcd. (%) for $C_{24}H_{16}O_4FCl$: C, 68.17; H, 3.81. Found: C, 68.24; H, 3.87.

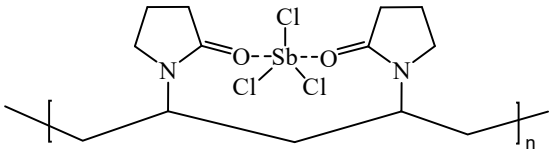
*3- (3- (4- chlorophenyl)- 1- (4- (dimethylamino)phenyl)- 3-oxopropyl)-4-hydroxy-2H-chromen-2-one (**3j**):*

White solid. m.p.= 176-178 °C. FT-IR (KBr): $\bar{\nu}$= 756, 815, 1095, 1207, 1398, 1456, 1517, 1564, 1618, 1654, 1699, 2854, 2920, 3436 cm^{-1}. ^{1}HNMR (400 MHz, $CDCl_3$): δ = 2.96 (s, 6H), 3.70 (dd, *J*= 19.0, 2.8 Hz, 1H), 4.35 (dd, *J*= 19.0, 9.6 Hz, 1H), 4.87 (dd, *J*= 9.6, 2.8 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 7.24-7.31 (m, 4H), 7.48-7.53 (m, 3H),7.96 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.40 (d, *J* = 8.8 Hz, 2H), 9.33 (s, 1H) ppm. ^{13}CNMR (100 MHz, $CDCl_3$): δ= 31.9, 34.6, 40.5, 40.6, 108.1, 112.5, 116.2, 116.7, 123.7, 123.8, 128.6, 128.8, 129.1, 130.0, 131.6, 134.3, 140.7, 149.4, 152.8, 160.6, 162.9, 201.6 ppm. Anal. Calcd. (%) for $C_{26}H_{22}NO_4Cl$: C, 69.72; H, 4.95, N, 3.13. Found: C, 70.02; H, 5.01, N, 3.17.

3. Results and Discussion

In this study, PVPP-$SbCl_3$ is obtained by a simple reaction of antimony(III) chloride with the polyvinylpolypyrrolidone (Scheme 2).

Characterization of the polyvinylpolypyrrolidone supported antimony(III) chloride was performed by recording the Fourier transform infrared spectroscopy (FT-IR) spectrum of PVPP-$SbCl_3$ (Fig. 1). For polyvinylpolypyrrolidone, the C-N stretch band, CH_2 bending band, the C=O stretch band, and the CH stretch band were found to be 1288 cm^{-1}, 1429 cm^{-1}, 1649 cm^{-1}, and 2956 cm^{-1} respectively (Fig. 1a). According to FT-IR analysis of PVPP-$SbCl_3$ indicated in Fig. 1b, the stretching vibrations of C=O for PVPP-$SbCl_3$ was



Scheme 2. The proposed chemical structure of PVPP-$SbCl_3$ complex.

observed at 1637 cm^{-1}. The good complexation of carbonyl functional groups of PVPP with 12 cm^{-1} red shift was observed for PVPP-$SbCl_3$. These results provided the evidences that antimony(III) chloride was successfully attached to the polyvinylpolypyrrolidone.

The thermal behavior of PVPP-$SbCl_3$ was shown in Fig. 2. The thermal analysis of PVPP-$SbCl_3$ showed two main decreasing peaks. First peak appears at temperature around 220–280 °C due to the loss of the antimony(III) chloride group from the polymer surface.

This is followed by a second peak at 320–370 °C, corresponding to the decomposition of the pyrrolidone functional group. The thermal analysis data showed that the catalyst is stable up to 200 °C.

Surface morphological study of PVPP–$SbCl_3$ was explored by scanning electron microscope (Fig. 3). The results of SEM analysis revealed that the $SbCl_3$ was properly dispersed within the PVPP matrix, which was directly related to good complexation between antimony(III) chloride and PVPP functional groups.

The elemental composition of the SEM image of PVPP–$SbCl_3$ is presented in Fig. 4. The EDX spectrum shows the presence of C, N, O, Sb and Cl in the catalyst. According to the EDX analysis, the antimony content in the catalyst was obtained 10.40 w%.

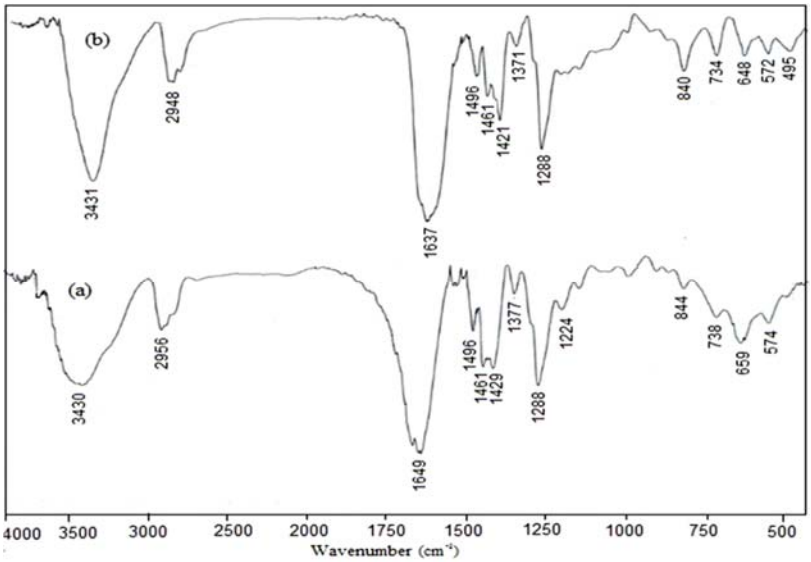


Fig. 1. FT-IR spectra of (a) PVPP, (b) PVPP-$SbCl_3$.

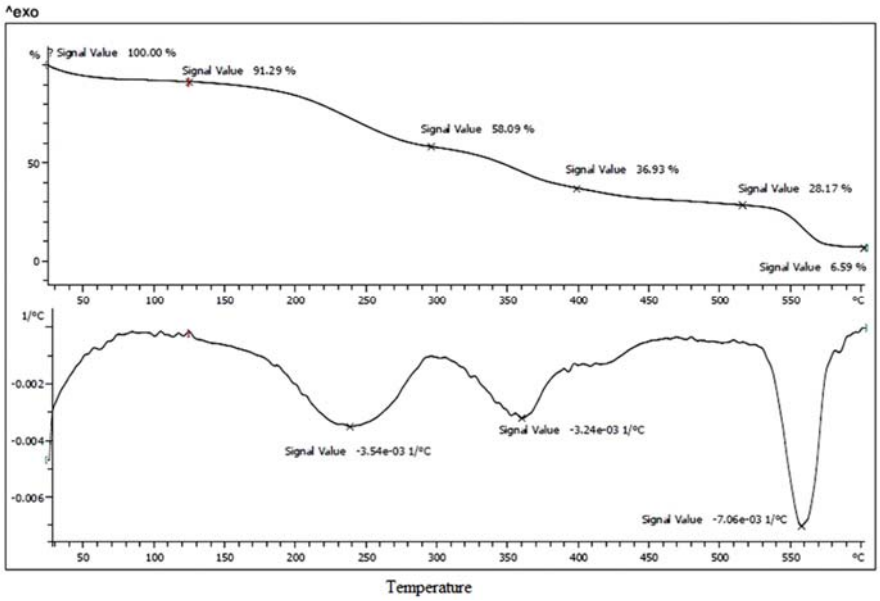


Fig. 2. The thermal analysis diagram of PVPP-$SbCl_3$.

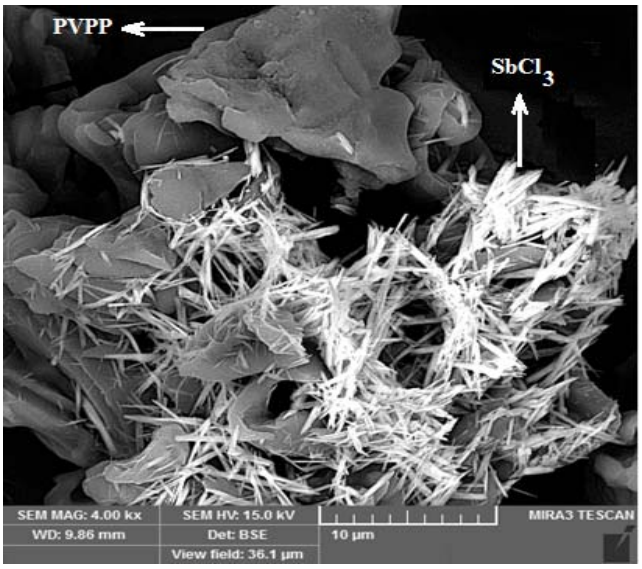


Fig. 3. SEM image of PVPP-$SbCl_3$.

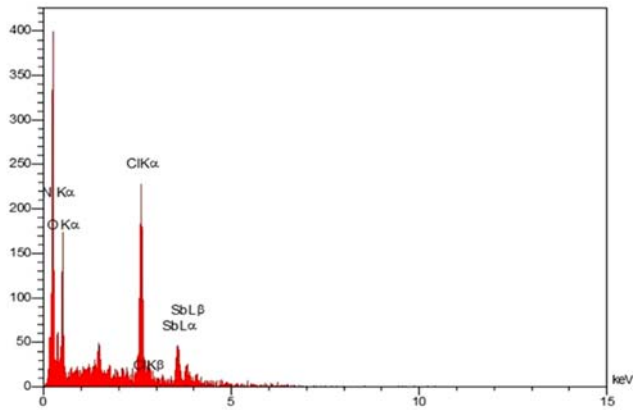


Fig. 4. The EDX spectrum of PVPP-$SbCl_3$.

In order to optimize the reaction conditions and get the best catalytic activity, the reaction of chalcone and 4-hydroxycoumarin was examined as a model reaction in the several catalysts. In this study, it was observed that polyvinylpolypyrrolidone-$SbCl_3$ in chloroform under reflux conditions is more efficient with respect to the reaction time and yields of the desired product (Table 1).

Furthermore, the reaction of chalcone and 4-hydroxycoumarin was examined in several solvents. In this investigation, it was perceived that $SbCl_3$ immobilized on polyvinylpolypyrrolidone in chlorform under reflux conditions is more efficient with respect to the reaction time and efficiency of the desired product (Table 2).

Table 1. Synthesis of **3a** in different catalysts.[a]

Entry	Catalyst	Amount (g)	Yield (%)[b]
1	nano-Fe_3O_4	0.057	70
2	nano-$ZnFe_2O_4$	0.06	65
3	nano-SnO_2	0.037	50
4	nano-MgO	0.01	42
5	nano-ZnO	0.02	45
6	$SbCl_3$	0.05	74
7	PVPP-$SbCl_3$	0.05	85

[a]Reaction conditions: Chalcone (1 mmol), 4-hydroxycoumarin (1 mmol) in $CHCl_3$ (5 mL) at reflux conditions after 4h.
[b]Isolated yields.

Table 2. Synthesis of **3a** in different solvents.[a]

Entry	Solvent	Yield (%)[b]
1	Solvent-free	30
2	n-hexane	20
3	EtOH (96%)	80
4	MeOH	60
5	EtOAc	40
6	$CHCl_3$	85

[a]Reaction conditions: Chalcone (1 mmol), 4-hydroxycoumarin (1 mmol), PVPP-$SbCl_3$ (0.05 g) at reflux conditions after 4h.
[b]Isolated yields.

After optimizing the reaction conditions, a diversity of chromenylphenylpropanones was synthesized using PVPP-$SbCl_3$ in good yields (Table 3, entries 1-10). The reactions worked well with all chalcones bearing electron-donating or electron-withdrawing substituent.

To check the reusability of the catalyst, it was employed in the synthesis of **3a**, four cycles under the optimum conditions. The catalyst powder was recovered by easy filtration and washed with dichloromethane. Then, according to the amount of catalyst, the required amount of fresh chalcone and 4-hydroxycoumarin were added. The results showed that the catalyst can be reused four consecutive times without significant loss of its catalytic activity (The yields were 85, 82, 80 and 78%, respectively).

In order to examine the efficiency of the present method for the synthesis of chromenylphenyl propanones, compound **3a** was compared with some of those reported in the literature (Table 4). Our results can be compared with previously reported data when all terms, including yields, reaction times, and reaction conditions are taken into account.

Table 3. Synthesis of chromenylphenylpropanones catalyzed by PVPP-$SbCl_3$.[a]

R	R′	Product	Time (h)	Yields (%)[b]	m.p. (°C)		Ref.
					Found	Reported	
H	H	**3a**	4	85	162-164	160-161	[8]
H	4-Cl	**3b**	3.5	83	177-179	179-181	[8]
4-Cl	H	**3c**	3.5	84	180-182	183-184	[10]
4-Br	H	**3d**	3.5	85	194-196	196-198	[10]
H	4-MeO	**3e**	4	74	176-177	175-178	[8]
3-NO_2	H	**3f**	3.5	82	187-189	----	
4-Cl	4-Cl	**3g**	3.5	86	154-156	156-157	[11]
4-MeO	H	**3h**	4	70	124-126	125-126	[9]
4-F	4-Cl	**3i**	3.5	84	184-186	----	
4-$(Me)_2N$	4-Cl	**3j**	4	75	176-178	----	

[a]Reaction and condition: Chalcones (1 mmol), 4-hydroxycoumarin (1 mmol), and PVPP-$SbCl_3$ (0.05 g) in chloroform (5 mL) at reflux conditions.
[b]All yields refer to isolated products.

Table 4. Comparison of PVPP-$SbCl_3$ with some other catalysts for synthesis of **3a**.

Entry	Catalyst	Reaction conditions	Time/h	Yield (%)	Ref.
1	-	H_2O/ reflux	57	26	[8]
2	4-pyrrolidinopyridine	$CHCl_3$/ reflux	24	62	[9]
3	-	EtOH/reflux	14	48	[11]
4	PVPP-$SbCl_3$	$CHCl_3$/ reflux	4	85	This work

4. Conclusions

In this study, we have extended a protocol for the synthesis of chromenylphenylpropanon derivatives as warfarine-like analogues by the reaction of 4-hydroxycoumarin with α,β-unsaturated compounds in the presence of polyvinylpolypyrrolidone supported antimony(III) chloride (PVPP-$SbCl_3$) as a reusable new polymeric Lewis acid catalyst in chloroform at reflux conditions.

Acknowledgements

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