

Polyaniline Salts and Complexes: Efficient and Reusable Catalyst for the One-Pot Synthesis of 5-(Methoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one

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ABSTRACT: Polyaniline salts were prepared by doping polyaniline base with different Bronsted acids (sulfuric, nitric, phosphoric, perchloric, hydrochloric acid) and organic acids (*p*-toluene sulfonic acid, 5-sulfosalicylic acid). Polyaniline complexes were also prepared using Lewis acids (aluminum chloride, ferric chloride). Polyaniline salts and polyaniline complexes were used as catalysts in Biginelli reaction for 5-(methoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one synthesis. Benzaldehyde and urea were reacted with methyl acetoacetate using polyaniline-*p*-toluene sulfonate salt as catalyst with different reaction time, temperature, and amount of catalyst. The use of polyaniline catalysts is feasible because of the easy preparation, easy handling, stability, easy recovery, simple work-up procedure, reusability, excellent activity with less amount of catalyst, and eco-friendly nature. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 102: 1741–1745, 2006

Key words: polyaniline catalyst; reusable catalyst; dihydropyrimidinone; Biginelli reaction

INTRODUCTION

Considerable attention has been paid to the potential of polymer-supported catalysts to act as heterogeneous and regenerable catalysts in organic transformations. Recently, polyaniline-supported metals (Pd, Pt, etc.)¹ and polyaniline-doped hetero poly acids (12-tungstosilicic acid, 12-molybdophosphoric acid)² are exhibiting catalytic activity in organic synthesis.

Several dihydropyrimidinones and their derivatives are pharmacologically potent calcium channel blocker,^{3,4} antihypertensive agents,^{5,6} α -adrenergic,^{7,8} and neuro-peptide Y (NPY) antagonists.⁹ These compounds also exhibit a broad range of biological activities¹⁰ such as antiviral, antitumor, antibacterial, anti-inflammatory properties, and act as a potent HIV gp-120-CD 4 inhibitor.¹¹

The synthesis of dihydropyrimidinones is currently important because of their wide range of pharmaceutical and biological properties. The most simple and straightforward procedure reported by Biginelli in 1893 involves one-pot condensation of ethyl acetoacetate, benzaldehyde, and urea under strongly acidic conditions.¹² However, the main draw back of Biginelli reaction is unsatisfactory yields obtained in the case of

substituted aromatic and aliphatic aldehydes. At present, several improved procedures have been reported such as Lewis acids,^{13–18} triflates,^{19–21} soluble polymer-supported liquid phase synthesis²² and we reported the use of polyaniline–bismoclite composite.²³ In recent years, the development of more economical and environmental friendly conversion process is gaining interest in the chemical community. In this article, we explored the possibility of use of polyaniline salts and complexes as polymeric reusable solid acid catalyst in the synthesis of dihydropyrimidinone.

EXPERIMENTAL

Materials

Aniline (reagent grade) from E. Merck was distilled prior to use. Reagent-grade sodium persulfate, benzaldehyde, methyl acetoacetate, urea, methanol, sulfuric, nitric, phosphoric, perchloric, hydrochloric acids, *p*-toluenesulfonic acid (PTSA), 5-sulfosalicylic acid (SSA), aluminum chloride, and ferric chloride (BDH, India) were used without further purification.

Preparation of polyaniline catalysts

Polyaniline salt and its base were prepared by aqueous polymerization pathway by previously reported procedure.^{24,25}

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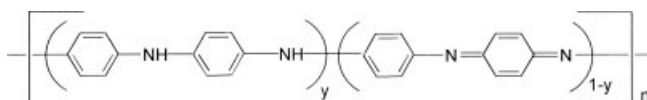


Figure 1 General structure of polyaniline base.

Polyaniline salt

In a 2-L round-bottomed flask, 700 mL of water was taken and 30 mL of H_2SO_4 was added slowly with stirring. To this solution, 10 mL of aniline was added and the solution was kept under constant stirring at 5–10°C. To this solution, 250 mL aqueous solution containing sodium persulfate (23.8 g) was added for 15–20 min duration. The reaction was allowed to continue for 4 h at 5–10°C. The precipitated polyaniline powder was filtered and washed with 5 L distilled water followed by 500 mL acetone. The polyaniline salt powder was dried at 100°C till a constant weight.

Polyaniline base

Polyaniline salt powder (7.0 g) synthesized by the aforementioned process was stirred in 700 mL aqueous sodium hydroxide solution (1.0M) for 8 h at ambient temperature. Polyaniline base powder was filtered, washed with water and finally with acetone and dried at 100°C till a constant weight.

Redoped polyaniline salt

50 mL of 1.0M solution of H_2SO_4 , HNO_3 , H_3PO_4 , HClO_4 , and HCl in water was prepared separately. In the case of PTSA, SSA, AlCl_3 , and FeCl_3 , 0.1M solution of acid was prepared in 50 mL acetone. Polyaniline base (0.5 g) was added to each of the above solution and kept under constant stirring at ambient temperature for 4 h. Solid was filtered, washed with ample of respective solvents and the solid was dried at 100°C till a constant weight.

Synthesis of 5-(methoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one

In a typical experiment, benzaldehyde (1.0 g, 9.43 mmol), methyl acetoacetate (1.22 g, 9.43 mmol), and urea (0.56 g, 9.43 mmol) was taken in 25-mL round-bottomed flask, and 10 mL of methanol was added followed by 50 mg of polyaniline-*p*-toluene sulfonate salt powder (5 wt % with respect to aldehyde). The reaction mixture was refluxed for 2 h. The reaction mixture was filtered at hot condition using Whatman 41 filter paper, and the methanol solvent was evaporated under vacuum. The crude product obtained was washed with water, filtered, and dried at 100°C. The product was purified by recrystallization using

methanol. The product was characterized by $^1\text{H-NMR}$, IR spectrum, and melting point.

5-(Methoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one

mp: 209–212°C; $^1\text{H-NMR}$ ($\text{CDCl}_3 + \text{DMSO-d}_6$): δ 9.08 (s, 1H), 7.30 (m, 5H), 5.30 (d, $J = 2.7$ Hz, 1H), 3.62 (s, 3H), 2.34 (s, 3H); $^{13}\text{C-NMR}$ (DMSO-d_6) δ 165.7, 152.0, 148.5, 144.6, 128.3, 127.2, 126.0, 98.9, 53.7, 50.7, 17.8; IR (KBr): 3360, 3240, 3090, 3030, 2945, 1720, 1640 cm^{-1} ; MS m/e 246 (20) 231 (28) 187 (27) 169 (100) 137 (40).

Characterization

$^1\text{H-NMR}$ spectrum for the obtained dihydropyrimidinone was recorded using Gemini-Varian 200 MHz equipment with CDCl_3 as solvent and TMS as an internal reference. $^{13}\text{C-NMR}$ spectrum was recorded using Bruker Avance 50 MHz spectrophotometer. IR spectrum was recorded using Perkin-Elmer Spectrometer. EI-mass spectrum was measured on VG Micro Mass 7070 H mass spectrometer. Melting point was found out using Mettler FP-51 Instrument. Polyaniline samples were pressed into disks of 16 mm diameter and ~ 2 mm thickness under a pressure of 400 MPa. Resistance measurement of the pellets was carried out on a two probe, connected to a Keithley Digital Multimeter (Model-2010). Resistance was calculated based on the average of at least three pairs of consistent readings at different points on the pressed pellet. Since, the mean value was used in the calculation of resistance, the total error involved is $< 1\%$.

RESULTS AND DISCUSSION

Polyanilines are particularly attractive because of their easy preparation, excellent electrical properties, number of intrinsic redox states, possible processability, and stability. The structure of polyaniline is known as *para*-linked phenylene amineimine. The base form of polyaniline (PANI) can, in principle, be shown in Figure 1.

In the generalized base form, $(1 - y)$ measures the function of oxidized units. When $(1 - y) = 0$, the polymer has no such oxidized groups and is commonly known as a leucoemeraldine base. The fully oxidized form, $(1 - y) = 1$, is referred to as a pernigraniline base. The half-oxidized polymer, where the

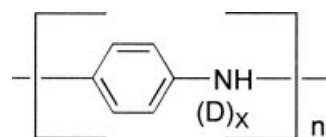


Figure 2 Simplified structure of polyaniline salt.

TABLE I
Physical and Electrical Properties of Polyaniline Salts and Polyaniline Complexes^{24,25}

Entry	Polyaniline system	Conductivity (S/cm)	Density (g/cm ³)	Dopant (%)	Dopant per aniline unit
1	PANI-H ₂ SO ₄	2.0×10^{-2}	1.22	23.3	0.29
2	PANI-HNO ₃	1.2×10^{-2}	1.21	18.7	0.34
3	PANI-H ₃ PO ₄	2.0×10^{-2}	1.23	29.5	0.32
4	PANI-HClO ₄	5.0×10^{-3}	1.21	25.7	0.32
5	PANI-HCl	5.0×10^{-4}	1.22	15.5	0.47
6	PANI-PTSA	1.0×10^{-2}	1.21	43.5	0.37
7	PANI-SSA	1.0×10^{-2}	1.29	25.3	0.12
8	PANI-AlCl ₃	6.0×10^{-4}	1.45	38.6	0.44
9	PANI-FeCl ₃	2.4×10^{-3}	0.96	27.3	0.22

number of reduced units and oxidized units are equal, i.e., $(1 - y) = 0.5$, is of special importance and is termed the emeraldine oxidation state or the emeraldine base. The emeraldine base is shown to be an alternating copolymer of reduced and oxidized repeat units. The value of y varies from 0 to 1, but the percentages of carbon, hydrogen, and nitrogen will be almost the same. Taking the above points into consideration, the formula of polyaniline salt given in Figure 2 is considered for simplicity.

Characterization of polyaniline

Polyaniline salts (PANI-HX, where PANI represents polyaniline and HX acid group) were prepared by doping polyaniline base with different Bronsted acids (H₂SO₄, HCl, HClO₄, HNO₃, H₃PO₄) and organic acids (PTSA, SSA). Polyaniline complexes were prepared using Lewis acids (AlCl₃ and FeCl₃). Polyaniline systems are well characterized and the results are reported in literature.^{24,25}

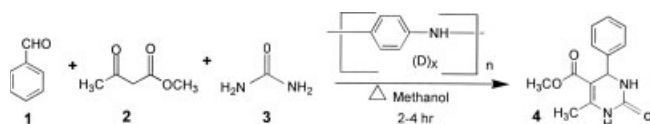
Physical and electrical properties

Amount of acid group (dopant, "D" in Fig. 2) present in the polyaniline chain was calculated based on the weight of redoped polyaniline salt obtained and the weight of polyaniline base used (Table I). Amount of dopant present in polyaniline system such as PANI-H₂SO₄, PANI-HClO₄, PANI-FeCl₃, and PANI-H₃PO₄ was found to be 23.3%, 25.7%, 27.3%, and 29.5% respectively. Higher amount of dopant was obtained in the case of PANI-AlCl₃ (38.6%) and PANI-PTSA (43.5%) and lower amount of dopant was observed in PANI-HCl and PANI-HNO₃ (15.5–18.7%). Acid

group per aniline unit ("x" in Fig. 2) was calculated from the amount of dopant present in the polyaniline chain and the values are included in Table I. Acid group per aniline unit was found to be almost same in the case of PANI-HNO₃, PANI-H₃PO₄, PANI-HClO₄, and PANI-PTSA (0.32–0.37). PANI-H₂SO₄ and PANI-FeCl₃ contains 0.29 and 0.22 acid group per aniline unit respectively. Higher amount of acid group per aniline unit was observed for PANI-AlCl₃ and PANI-HCl (0.44–0.47) and lower amount of acid group per aniline unit was obtained for PANI-SSA (0.12). Density of all polyaniline salts was found to be nearly the same (1.21–1.29 g/cm³). However, density of the polyaniline complexes depends upon the density of Lewis acid dopant. PANI-AlCl₃ has very high density (1.45 g/cm³) and PANI-FeCl₃ is having very low density (0.96 g/cm³; Table I). Conductivity of PANI-H₂SO₄, PANI-HNO₃, PANI-H₃PO₄, PANI-PTSA, and PANI-SSA systems were found to be nearly the same (10^{-2} S/cm). Lower conductivities were observed in case of PANI-HClO₄ (5.0×10^{-3} S/cm), PANI-HCl (5.0×10^{-4} S/cm), PANI-AlCl₃ (6.0×10^{-4} S/cm), and PANI-FeCl₃ (2.4×10^{-3} S/cm).

TABLE II
Synthesis of Dihydropyrimidinone by Varying Reaction Time, Temperature, and Catalyst Amount (PANI-PTSA Catalyst)

Entry	Time (h)	Temperature (°C)	Amount of catalyst (wt %)	Yield (%)
1	0.5	64	5	42
2	1.0	64	5	62
3	1.5	64	5	82
4	2.0	64	5	97
5	16	RT	5	Nil
6	16	40	5	Nil
7	16	50	5	28
8	2	64	1.0	22
9	2	64	2.5	36
10	2	64	5.0	97
11	2	64	7.5	97
12	2	64	10	97



Scheme 1 Synthesis of dihydropyrimidinone.

TABLE III
Synthesis of Dihydropyrimidinone Using Various Catalysts and Their Reusability

Entry	Type of the catalyst	Amount of the catalyst (wt %)	Time (h)	Yield (%)	Reusability checked (No. of times)
1	Polyaniline-sulfate	10	3	95–97	4
2	Polyaniline-nitrate	10	4	94–97	3
3	Polyaniline-phosphate	10	4	92–96	3
4	Polyaniline-perchlorate	10	3	94–97	3
5	Polyaniline-hydrochloride	10	4	93–94	3
6	Polyaniline- <i>p</i> -toluene sulfonate	5	2	97–98	7
7	Polyaniline-sulfosalicylate	10	3	94–96	3
8	Polyaniline-aluminum chloride	5	2	97–98	4
9	Polyaniline-ferric chloride	5	2	90–93	3

Investigation of synthesis conditions of dihydropyrimidinone using PANI-PTSA catalyst

The cyclic condensation reaction between benzaldehyde, methyl acetoacetate, and urea was carried out at methanol reflux temperature (64°C) using polyaniline salt catalysts (Scheme 1).

The reaction was carried out using 5 wt % PANI-PTSA catalyst with different time and the yield of dihydropyrimidinone was increased as 42%, 62%, 82%, and 97% with increase in time from 0.5 to 2.0 h (Table II, entries 1–4). The reaction was also carried out at different temperatures and 97% yield of dihydropyrimidinone was obtained at 64°C. However, product was not formed when the reaction was carried out at 30°C and 40°C for 16 h and less amount of product (28%) was obtained at 50°C (Table II, entries 5–7). The yield of the product was increased as 22%, 36%, and 97% with the use of 1.0, 2.5, and 5.0 wt % of PANI-PTSA salt and maintained constant yield (97%) with increasing amount of catalyst from 7.5–10 wt % (Table II, entries 8–12).

Investigation of polyaniline catalyst efficiency

The cyclic condensation reaction was carried out between benzaldehyde, methyl acetoacetate, and urea in the presence of various polyaniline salts and complexes as catalyst and excellent yields were obtained (90–97%, Table III). The mechanism of the reaction would be similar to the acid catalyst reaction reported by Kappe.²⁶ Polyaniline salts and complexes used in the present study underwent smooth and clean reaction and the formation of product was found to be independent of the amount of acid present in polyaniline chain as well as the strength of acid. For example, dihydropyrimidinone was obtained in almost the same yield (93–98%) with the use of PANI-PTSA and PANI-HCl catalysts (Table III). However, PANI-PTSA contains 43.5 wt % of PTSA whereas PANI-HCl contains 15.5 wt % only (Table I). Polyaniline salts and polyaniline complexes could be used as catalysts in dihydropyrimidinone synthesis.

Reusability of the catalyst

Reusability of the catalyst was checked by the condensation with benzaldehyde, methyl acetoacetate, and urea using PANI-PTSA catalyst in methanol medium, which results in 98% yield. The PANI-PTSA was recovered and reused for a further seven times and resulted in 96–98% yields. The recovered catalyst was subjected for infrared, XRD analysis, conductivity measurements, and amount of PTSA present in polyaniline salt. Similar infrared, XRD pattern, and conductivity were observed for PANI-PTSA salt before and after catalytic reaction. The amount of PTSA present in polyaniline sulfate salt was found to be almost the same before (43.5 wt %) and after the catalytic reaction (43.4 wt %). These results are indicating that PANI-PTSA salt catalyst does not lose its activity and can be reused. In the case of PANI-PTSA catalyst, the reusability reaction was checked seven times and in other polyaniline catalyst systems, the reusability property was checked for three to four times.

CONCLUSIONS

The synthesis of dihydropyrimidinone catalyzed by regenerable polyaniline salts and complexes is noteworthy because polyaniline salts and complexes act as catalyst and underwent smooth, clean reaction with simple work-up procedure. This method has several advantages; the catalytic use of polyaniline salt is quite feasible because of its easy preparation, easy handling, stability, easy recovery, reusability, and eco-friendly nature.

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