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Note

Facile $ZrCl_4$ promoted four-component coupling one-pot synthesis of polyhydroquinoline derivatives through unsymmetric Hantzsch reaction

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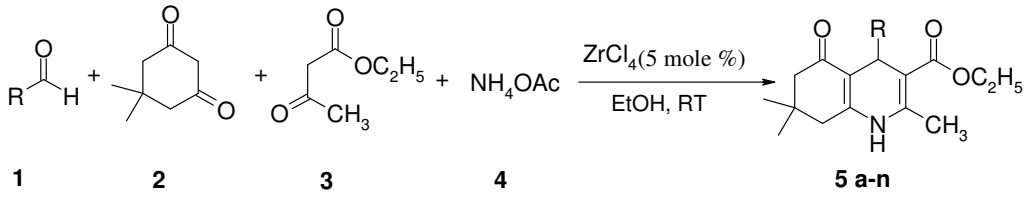
$ZrCl_4$ catalyzed efficient unsymmetric Hantzsch reaction *via* four-component coupling reaction of aldehydes, dimedone, ethyl acetoacetate and ammonium acetate at ambient temperature is described as the preparation of polyhydroquinoline derivatives. The process presented here is an operationally simple, economic, environmentally benign and provides excellent yield. Furthermore, the catalyst can be recovered conveniently and reused efficiently.

Keywords: Polyhydroquinolines, four-component coupling, one-pot conversion, $ZrCl_4$ catalyst

4-Substituted 1,4-dihydropyridines (1,4-DHPs) are well known as calcium channel modulators and have emerged as one of the most important classes of drugs for the treatment of cardiovascular diseases[1]. Cardiovascular agents such as nifedipine, nicardipine, amlodipine, and other related derivatives are dihydropyridyl compounds, effective in treatment of hypertension[2]. 1,4-Dihydropyridine derivatives possess a variety of biological properties such as vasodilator, bronchodilator, antiatherosclerotic, antitumor, geroprotective, hepatoprotective, and antidiabetic activity[3]. Recent studies have revealed that 1,4-DHPs exhibit various medicinal functions such as neuroprotectant, platelet anti-aggregatory activity, cerebral antischemic activity in the treatment of Alzheimer's disease and chemosensitizer in tumor therapy[4]. These examples clearly demonstrate the remarkable potential of novel DHP derivatives as a source of valuable drug candidates. A recent computational analysis of the comprehensive medicinal chemistry database showed the DHP framework to be among the most prolific chemo-types found. Development of drug resistance, both intrinsic and acquired drug resistance, remains a clinical obstacle in the chemotherapy of many cancers[5,6]. Among the possible resistance modifiers, the dihydropyridines, calcium antagonists, have been studied extensively as the analogue of verapamil[7]. Furthermore, the oxidation of these compounds to pyridines has also been studied[8-10]. Relatively speaking 1,4-dihydropyridine derivatives combined with a single ring have been mostly reported. Thus, the synthesis of heterocyclic nucleus is of continuing interest.

In view of the importance of polyhydroquinoline derivatives, many classical methods for their synthesis were reported[11-13], using conventional heating and refluxing approaches in the presence of an organic solvent. These methods, however, suffer from several drawbacks such as long reaction times, use of large quantities of volatile organic solvents, low yields, and harsh reaction conditions. Therefore, it is necessary to develop an efficient and versatile method for the preparation of these compounds. Recently several methods have been reported comprising the use of microwave[14], TMSI[15], ionic liquids[16,17], metal triflates[18], $HClO_4$-SiO_2[19], organocatalysts[20] and polymers[21,22]. However, the use of high temperatures, expensive metal precursors, catalysts that are harmful to environment, and longer reaction times limit the use of these methods. Therefore, the search for a better catalyst for the synthesis of polyhydroquinoline derivatives using less hazardous solvent or solvent-free conditions is of prime importance.

In continuation of our interest in developing novel synthetic methodologies[23] and use of transition metal salts as environmentally friendly reagents for organic synthesis, we undertook a study of the utility of transition metal salt like $ZrCl_4$ as a catalyst for the synthesis of polyhydroquinoline derivatives. Zr^{4+} with a high charge-to-size ratio (22.22 e^2 m^{-10}, ref. 24) enables reactions with high to excellent yields due to strong coordination ability of Zr^{4+}. Additionally, many advantages such as low cost, eco-friendly nature, ease of handling, non-toxicity (LD_{50}, oral rat = 1688 mg kg^{-1}, ref. 25), high reactivity make $ZrCl_4$ a potent catalyst in the synthetic transformations[26]. Therefore, the application of $ZrCl_4$ in organic synthesis is of renewed interest. Moreover, to the best of our knowledge no report has been made sofar about



Scheme I

the use of $ZrCl_4$ as catalyst in the Hantzsch condensation. We, therefore, were interested in exploiting the catalytic activity of $ZrCl_4$ in the synthesis of polyhydroquinoline derivatives through unsymmetric Hantzsch reaction.

Results and Discussion

Herein, the studies of a facile four-component unsymmetric Hantzsch condensation in the presence of $ZrCl_4$ catalyst at room temperature using substituted aldehydes **1**, dimedone **2**, ethyl acetoacetate **3**, and ammonium acetate **4**, to produce the polyhydroquinoline derivatives **5**, in excellent yields (**Scheme I**) is reported.

In a typical experimental procedure using traditional conditions, a solution of dimedone, a substituted aldehyde, ethyl acetoacetate, and ammonium acetate in ethyl alcohol was stirred in the presence of a catalytic amount of $ZrCl_4$ (5 mole%) for a certain period of time required to complete the reaction (TLC), resulting in the formation of the corresponding polyhydroquinoline. The reaction-mixture was then poured into brine solution and extracted with ethylacetate. The organic layer was dried over anhyd. sodium sulfate and evaporated to give crude product. The pure product was obtained by recrystallization from methanol. The reactions without any catalyst was also carried out but the polyhydroquinoline derivatives were isolated in poor yields (10-15%), and the major product isolated was a dimedone aldehyde adduct.

After the reaction was completed, the product was filtered directly and the catalyst was extracted by water from the residue. $ZrCl_4$ is more soluble in water than that in organic solvents. The catalyst could be recovered almost quantitatively from aqueous layer, which was subsequently reused several times. The results indicated, no loss of activity after three successive runs. The yields obtained were 94, 92 and 89% in the first, second and third run respectively.

The scope and generality of this four-component coupling one-pot synthesis of polyhydroquinoline derivatives through unsymmetric Hantzsch reaction is illustrated with different aldehydes and the results are summarized in **Table I.** This method has the ability to tolerate a variety of functional groups such as hydroxyl, methoxy, methyl, nitro, halides, olefins etc., under the reaction conditions. Both, the electron-rich and electron-deficient aldehydes as well as heterocyclic aldehyde (furfural) worked well, leading to high yields of product. All the products were identified by comparison of analytical data (m.p, IR and NMR) with those of authentic samples.

The use of 5 mole% of $ZrCl_4$ in stirring ethanol is sufficient to push the reaction forward. Higher amounts of $ZrCl_4$ did not lead to significant improvement in the yield of polyhydroquinolines. In ethanol medium the reaction was complete within 2-4 hr at RT, whereas under reflux conditions the reaction was complete within 1 hr.

Under solvent free conditions, though the reaction proceeded quickly but was associated with many other by-products. The reaction using different solvents was also studied. In each case, the reactants were mixed together with 5 mole% $ZrCl_4$ stirred with 5 mL solvent. The polar solvents such as ethanol and acetonitrile were found to be better solvents than the non-polar solvents like toluene, methylene chloride, cyclohexane etc. Obviously, the results could be attributed to the better solubility of the catalyst and the reagents in the polar solvents. Among the two solvents *viz*., ethanol and acetonitrile, ethanol stands out as the solvent of choice, with its fast conversion, high yield and low toxicity.

To show the merit of the present work in comparison with other reported results in the literature, we compared the results of $ZrCl_4$ with other catalysts used in the synthesis of polyhydroquinoline derivatives (**Table II**). It was found that the conventional Lewis acids such as $AlCl_3$ and $FeCl_3$ showed poor yield of the product. Even with large amounts of catalyst used, the results were unsatisfactory and many side reactions were observed whereas $ZrCl_4$ acts as an effective catalyst. The yields of the polyhydroquinoline derivatives **5a-n** ranged

Table I — $ZrCl_4$ promoted one-pot synthesis of polyhydroquinoline derivatives[a]

Entry	R	Time (hr)	Yield (%)[b]	Product/Product characterization data
5a	C_6H_5	2.0	94	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-phenyl-5-(*6H*)-oxoquinoline-3-carboxylate 5a**. m.p. 202-04 °C (Lit. 203-04 °C, ref. 19); IR (KBr): 3287, 3077, 2964, 1696, 1610 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.93 (s, 3H), 1.06 (s, 3H), 1.20 (t, 3H, *J* = 7.1 Hz), 2.12-2.28 (m, 4H), 2.34 (s, 3H), 4.05 (q, 2H, *J* = 7.1 Hz), 5.06 (s, 1H), 6.63 (s, 1H), 7.07-7.12 (m, 1H), 7.17-7.22 (m, 2H), 7.27-7.32 (m, 2H).
5b	4-OH-C_6H_4	4.0	89	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-hydroxyphenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5b**. m.p. 232-34 °C (Lit. 233-34 °C, ref. 18); IR (KBr): 3390, 2955, 1700, 1645, 1590, 1480, 1385, 1220, 782 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, 3H, *J* = 7.2 Hz), 2.09-2.19 (m, 3H), 2.20-2.34 (m, 4H), 4.06 (q, 2H *J* = 7.6 Hz), 4.98 (s, 1H), 5.61, (s, 1H), 6.65 (d, 2H, *J* = 8.9 Hz), 7.17 (d, 2H, *J* = 8.4 Hz).
5c	4-CH_3O-C_6H_4	2.0	93	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-methoxyphenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5c**. m.p. 255-57 °C (Lit. 256-57 °C, ref. 18); IR (KBr): 3275, 2957, 1705, 1647, 1605, 1497, 1382, 1217, 1032, 766 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$ +DMSO-d_6): δ 0.93 (s, 3H), 1.08 (s, 3H), 1.22 (t, 3H, *J* = 7.2 Hz), 2.02-2.11 (m, 4H), 2.31 (s, 3H), 3.73 (s, 3H), 4.01 (q, 2H *J* = 7.2 Hz), 4.81 (s, 1H), 6.64 (d, 2H, *J* = 7.3 Hz), 7.11 (d, 2H, *J* = 7.3 Hz), 8.64 (s, 1H).
5d	4-CH_3-C_6H_4	2.0	94	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-methylphenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5d**. m.p. 260-62 °C (Lit. 261-62 °C, ref. 19); IR (KBr): 3275, 3080, 2960, 1700, 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.95 (s, 3H), 1.08 (s, 3H), 1.21 (t, 3H, *J* = 7.1 Hz), 2.12-2.27 (m, 7H), 2.33 (s, 3H), 4.05 (q, 2H, *J* = 7.1 Hz), 5.02 (s, 1H), 6.65 (s, 1H), 7.00 (d, 2H, *J* = 7.9 Hz), 7.18 (d, 2H, *J* = 7.9 Hz).
5e	4-F-C_6H_4	3.0	92	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-fluorophenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5e**. m.p. 184-86 °C (Lit. 185-86 °C, ref. 19); IR (KBr): 3290, 2960, 1695, 1610, 1490, 1380, 1220, 1025, 764 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.93 (s, 3H), 1.08 (s, 3H), 1.19 (t, 3H, *J* = 7.3 Hz), 2.12-2.26 (m, 4H), 2.37 (s, 3H), 4.06 (q, 2H, *J* = 7.3 Hz), 5.02 (s, 1H), 5.81, (s, 1H), 6.86-6.90 (m, 2H), 7.22-7.28 (m, 2H).
5f	2-Cl-C_6H_4	2.5	89	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(2-chlorophenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5f**. m.p. 206-08 °C (Lit. 207-08 °C, ref. 19); IR (KBr): 3062, 2955, 1720, 1640, 1610, 1468, 1385, 1228, 1020, 745 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.94 (s, 3H), 1.06 (s, 3H), 1.20 (t, 3H, *J* = 7.2 Hz), 2.02-2.20 (m, 4H), 2.39 (s, 3H), 4.05 (q, 2H, *J* = 7.2 Hz), 4.61 (s, 1H), 7.11-7.30 (m, 4H), 7.61 (s, 1H).
5g	4-Cl-C_6H_4	2.0	88	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-chlorophenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5g**. m.p. 244-46 °C (Lit. 245-46 °C, ref. 19); IR (KBr): 3275, 3200, 3075, 2965, 1705, 1650, 1605 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.94 (s, 3H), 1.08 (s, 3H), 1.19 (t, 3H, *J* = 7.1 Hz), 2.12-2.35 (m, 4H), 2.36 (s, 3H), 4.05 (q, 2H, *J* = 7.1 Hz), 5.03 (s, 1H), 6.46 (s, 1H), 7.15-7.20 (m, 2H), 7.25-7.27 (m, 2H).
5h	3-NO_2-C_6H_4	2.0	84	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(3-nitrophenyl)-5-(*6H*)-oxoquinoline-3-carbxylate 5h**. m.p. 178-80 °C (Lit. 178-79 °C, ref. 19); IR (KBr): 3285, 3210, 3080, 2960, 1705, 1605, 1530 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.93 (s, 3H), 1.08 (s, 3H), 1.21 (t, 3H, *J* = 7.1 Hz), 2.12-2.41 (m, 7H), 3.68 (q, 2H, *J* = 7.1Hz), 5.15 (s, 1H), 6.86 (s, 1H), 7.35 (t, 1H *J* = 7.9 Hz), 7.72 (d, 1H, *J* = 7.9 Hz); 7.96 (m, 1H), 7.98 (m, 1H).
5i	3,4-Cl_2-C_6H_3	2.5	85	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(3,4-dichlorophenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5i**. m.p. 214-16 °C (Lit. 213-15 °C, ref. 20); IR (KBr): 3282, 3080, 2960, 1710, 1650, 1600, 1490 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.83 (s, 3H), 1.08 (s, 3H), 1.22 (t, 3H, *J* = 7.1 Hz), 2.13-2.39 (m, 7H), 4.04 (q, 2H, *J* = 7.1Hz), 5.03 (s, 1H), 6.42 (s, 1H), 7.18 (m, 1H), 7.27, (m, 1H), 7.35 (d, 1H, *J* = 2.0 Hz).
5j	3,4-$(OCH_3)_2$-C_6H_3	3.0	93	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(3,4-dimethoxyphenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5j**. m.p. 197-99 °C (Lit. 198-99 °C, ref. 19); IR (KBr): 3240, 2955, 1694, 1645, 1610, 1490, 1380, 1217, 1027, 753 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.95 (s, 3H), 1.08 (s, 3H), 1.21 (t, 3H, *J* = 7.3 Hz), 2.19-2.35 (m, 4H), 2.38 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 4.07 (q, 2H, *J* = 7.3), 5.03 (s, 1H), 5.92 (s, 1H), 6.69 (d, 1H, *J* = 8.30 Hz), 6.77 (dd, 1H, *J* = 8.30, and 1.96 Hz), 6.93 (d, 1H, *J* = 1.96).

—Contd

Table I — $ZrCl_4$ promoted one-pot synthesis of polyhydroquinoline derivatives[a]—*Contd*

Entry	R	Time (hr)	Yield (%)[b]	Product/Product characterization data
5i	3,4-Cl_2-C_6H_3	2.5	85	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(3,4-dichlorophenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5i**. m.p. 214-16 °C (Lit. 213-15 °C, ref. 20); IR (KBr): 3282, 3080, 2960, 1710, 1650, 1600, 1490 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.83 (s, 3H), 1.08 (s, 3H), 1.22 (t, 3H, *J* = 7.1 Hz), 2.13-2.39 (m, 7H), 4.04 (q, 2H, *J* = 7.1Hz), 5.03 (s, 1H), 6.42 (s, 1H), 7.18 (m, 1H), 7.27, (m, 1H), 7.35 (d, 1H, *J* = 2.0 Hz).
5j	3,4-$(OCH_3)_2$-C_6H_3	3.0	93	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(3,4-dimethoxyphenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5j**. m.p. 197-99 °C (Lit. 198-99 °C, ref. 19); IR (KBr): 3240, 2955, 1694, 1645, 1610, 1490, 1380, 1217, 1027, 753 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.95 (s, 3H), 1.08 (s, 3H), 1.21 (t, 3H, *J* = 7.3 Hz), 2.19-2.35 (m, 4H), 2.38 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 4.07 (q, 2H, *J* = 7.3), 5.03 (s, 1H), 5.92 (s, 1H), 6.69 (d, 1H, *J* = 8.30 Hz), 6.77 (dd, 1H, *J* = 8.30, and 1.96 Hz), 6.93 (d, 1H, *J* = 1.96).
5k	4-OH, 3-OCH_3-C_6H_3	2.5	92	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-hydroxy-3-methoxyphenyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5k**. m.p. 211-12 °C (Lit. 211-12 °C, ref. 19); IR (KBr): 3390, 2955, 1700, 1645, 1590, 1480, 1385, 1220, 1030, 782 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.95 (s, 3H), 1.09 (s, 3H), 1.24 (t, 3H, *J* = 7.2 Hz), 2.02-2.20 (m, 4H), 2.30 (s, 3H), 3.81 (s, 3H), 4.06 (q, 2H, *J* = 7.2), 4.81 (s, 1H), 6.61 (s, 2H), 6.83 (s 1H), 7.69 (s, 1H), 8.50 (s, 1H).
5l	C_6H_5CH=CH	4.0	91	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-cinnamyl-5-(*6H*)-oxoquinoline-3-carboxylate 5l**. m.p. 204-06 °C (Lit. 204-06 °C, ref. 18); IR (KBr): 3300, 2965, 1675, 1602, 1483 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.09 (s, 3H), 1.11 (s, 3H), 1.24-1.31 (m, 3H), 2.28 (t, 3H, *J* = 7.3 Hz), 2.33-2.37 (m, 4H), 4.11-4.20 (m, 2H), 4.70 (d, 1H, *J* = 7.0 Hz), 5.75 (s, 1H), 6.21 (d, 2H, *J* = 7.1 Hz), 7.22-7.30 (m, 5H).
5m	4-OCH_3-C_6H_4CH=CH	4.0	91	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(4-methoxycinnamyl)-5-(*6H*)-oxoquinoline-3-carboxylate 5m**. m.p. 199-201 °C (Lit. 198-200 °C, ref. 20); IR (KBr): 3302, 2963, 1674, 1603, 1484 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.09 (s, 3H), 1.13 (s, 3H), 1.26 (t, 3H, *J* = 7.1 Hz), 2.18-2.33 (m, 4H), 2.38 (s, 3H), 3.77(s,3H) 4.13-4.27 (m, 2H), 4.72 (d, 1H, *J* = 6.1), 6.17 (dd, 1H, *J* = 16.2 and 6.1 Hz) 6.46 (s, 1H), 6.59 (d, 1H, *J* = 16.2 Hz), 6.79-6.89 (m, 2H), 7.11-7.17 (m, 1H), 7.38 (d, 1H, *J* =1.3 Hz).
5n	2-furyl	2.0	92	**Ethyl 1,4,7,8-tetrahydro-2,7,7-trimethyl-4-(2-furyl) -5-(*6H*)-oxoquinoline-3-carboxylate 5n**. m.p. 245-47 °C (Lit. 246-48 °C, ref. 18); IR (KBr): 3288, 3078, 2969, 1687, 1602, 1493, 1034, 941, 877, 826 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.03 (s, 3H), 1.12 (s, 3H), 1.26 (t, 3H, *J* = 6.9 Hz), 2.21-2.27 (m, 3H), 2.35-2.38 (m, 4H), 4.10-4.18 (m, 2H), 5.25 (s, 1H), 5.80 (s, 1H), 6.02 (s, 1H), 6.20 (s, 1H), 7.17 (s, 1H).

[a]All the reactions were carried at RT
[b]Isolated yield

Table II — Comparison of the yields of polyhydroquinolines in the presence of different catalysts[a]

Entry	Catalyst	Amount of catalyst (mole %)	Time (hr)	Yield (%)[b]
1	$AlCl_3$[18]	200	12	43
2	$FeCl_3$[18]	200	12	48
3	$ZnCl_2$[18]	150	12	42
4	$NdCl_3$[18]	25	12	76
5	$Yb(OTf)_3$[18]	5	5	90
6	L-Proline[20]	10	2	85
7	$ZrCl_4$	5	2	94

[a]Hantzsch reaction of benzaldehyde, ethyl acetoacetate, dimedone and ammonium acetate in ethanol at RT.
[b]Isolated pure product yield.

from 84 to 94%, which are, far the most past, significantly higher than previously reported.

In conclusion, it is demonstrated that the four-component Hantzsch reaction can effectively be performed with $ZrCl_4$, which provides a simple and efficient method for the synthesis of polyhydroquinoline derivatives. The present method offers many advantages such as generality, simplicity, avoids use of harmful organic solvents and effective recycling of the catalyst compared to those reported in the literature.

Experimental Section

All the reagents were purchased from Sigma-Aldrich Chemical Company or Lancaster and were

used directly without further purification. Melting points were determined in open capillaries and are uncorrected. IR spectra (KBr) were recorded on a Perkin-Elmer spectrum BX series FT-IR spectrometer. ^{1}H NMR spectra were obtained on a Varian Gemini (200 MHz) spectrometer in $CDCl_3$ using TMS as internal reference. TLC was carried out on GF_{254} silica gel plates.

General procedure for the preparation of poly-hydroquinolines 5a-n

To a stirred mixture of dimedone (1 mmole), ethyl acetoacetate (1 mmole) and $ZrCl_4$ (5 mole%) in ethanol (5 mL), aldehyde (1 mmole) and ammonium acetate (1 mmole) were added at ambient temperature. The reaction-mixture was stirred at room temperature until the reaction was completed (monitored by TLC). The resulting yellow solid product was filtered, treated with water followed by brine solution and extracted with ethyl acetate. The organic layer was dried over anhyd. sodium sulfate and evaporated to dryness to afford the crude product. The pure product was obtained by further recrystallization using methanol. The filtrate was concentrated, diluted with ethylacetate, washed with water and the aqueous layer containing the catalyst was evaporated under reduced pressure to give a white solid (catalyst), which was reused.

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