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Vanadium dodecylamino phosphate: A novel efficient catalyst for synthesis of polyhydroquinolines

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A novel vanadium dodecylamino phosphate was synthesised by an instant reaction between phosphoric acid and vanadyl acetylacetonoate using dodecylamine as the structure-directing agent at ambient temperature. The physicochemical characteristics of the material were investigated by a variety of analytical techniques. XRD studies revealed the presence of vanadium phosphate and hydrated vanadium phosphate phases in the framework of the material. The catalytic application of this material toward in the synthesis of polyhydroquinolines via Hantzsch condensation was investigated at ambient temperature. This method affords high yields within short reaction times. The influence of various reaction parameters such as different solvents, catalyst dosage, effect of aldehydes, and reusability was studied and a plausible mechanism proposed.

Keywords: vanadium, dodecylamine, Hantzsch condensation, polyhydroquinolines

Introduction

Quinolines, having a 1,4-dihydropyridine nucleus (1,4-DHPs), are important bioactive compounds, well-known Ca^{2+} channel-blockers and analogues of NADH coenzymes. 1,4-DHPs exhibit a variety of pharmacological properties such as anti-malarial, anti-inflammatory, anti-asthmatic, and antibacterial activities, as well as being tyrosine kinase- inhibiting agents (Chen et al., 2001). The heterocyclic rings of 1,4-DHP function biologically as vasodilators, bronchodilators, anti-atherosclerotic, anti-tumour, geroprotective, hepatoprotective, and anti-diabetic agents and for the treatment of cardiovascular diseases (Shan et al., 2004). Dihydropyridyl-based cardiovascular agents which are effective in the treatment of hypertension include nifedipine, nicardipine, amlodipine, and other related derivatives (Heydari et al., 2009). Studies reveal that 1,4-DHPs present a number of medicinal applications, e.g., as a neuroprotectant, platelet anti-aggregatory agent, chemo sensitiser in tumour therapy, and cerebral anti-ischemic agent in the treatment of Alzheimer's disease (Kumar et al., 2008). In view of the overall biological importance of 1,4-DHPs as a valuable drug in pharmacological applications, several methods have been reported for their synthesis.

Standard methods such as refluxing in acetic acid or in alcohol have been reported for the synthesis of these derivatives. However, these methods suffer from drawbacks such as long reaction times, harsh refluxing conditions, use of large quantities of organic solvents, and low product yields. A survey of the literature reveals a number of homogeneous and heterogeneous catalytic systems in use for the synthesis of polyhydroquinoline derivatives, including the use of microwaves, autoclave, TMSCl-NaI (Sabitha et al., 2003a), ionic liquids (Ji et al., 2004), $InCl_3$, Cs-Norit carbons (Perozo-Rondon et al., 2006), molecular iodine (Ko et al., 2005), metal triflates (Wang et al., 2005), organocatalyst, tris(pentafluorophenyl)borane (Chandrasekhar et al., 2008), ceric ammonium nitrate, $HClO_4$–SiO_2, silica sulphuric acid (Kolvari et al., 2011), L-proline and

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*Corresponding author, e-mail: venkatathrin@yahoo.com derivatives, potassium dodecatungstocobaltate trihydrate (Nagarapu et al., 2008), HY zeolite (Das et al., 2006), montmorillonite K-10 (Song et al., 2005), heteropoly acid, molybdenum(VI) complex, tetrabutylammonium hydrogen sulphate, fluoroboric acid (Chen et al., 2007), boronic acids, nickel nanoparticle, PTSA-SDS, BINOL-phosphoric acid derivatives (Evans & Gestwicki, 2009), and hafnium(IV) bis(perfluorooctanesulphonyl)imide complex (Hong et al., 2010). However, some of the above methods have their limitations in terms of yields, elevated temperatures, extended reaction times, difficult procedures, and the use of expensive reagents. In some cases, the catalysts in use are acidic or basic and are harmful to the environment.

Hence, it was desirable to develop a new and convenient method for the synthesis of polyhydroquinolines. All of the above disadvantages reflect the need for further improvements to the synthesis of new economically viable catalysts.

Phosphates are effective in several industrial acid-based reactions (Samantaray et al., 2000). The phosphates appear to enhance the catalytic properties, stabilise the surface area and crystal phase, improve the surface acidity, and render the material porous. Metal phosphates also attract interest for their practical applications in areas such as catalysis, ion exchange, intercalation chemistry, proton conduction, optical and electromagnetic functional materials (Das & Parida, 2008). Among the various metal phosphates, vanadium phosphates (VPO) are of interest due to their exceptional structures, interesting host–guest chemistry, and potential applications in catalysis. VPOs are layered compounds and have found many applications in materials science and as heterogeneous catalysts in various oxidation reactions (Solsona et al., 2003). Vanadium-containing microporous molecular sieves were found to be active in a number of oxidation reactions (Whittington & Anderson, 1993). They are extremely important in heterogeneous catalysis for the selective oxidation of *o*-xylene to phthalic anhydride (Dias et al., 1997), methane and methanol to formaldehyde, benzyl alcohol to benzaldehyde, esterification of oleic acid, ammoximation of aromatics and alkyl aromatics (Cavani et al., 1987), butane to maleic anhydride (Bergman & Frisch, 1966), propane to acrylic acid (Gribot-Perrin et al., 1996), oxidative dehydrogenation of ethane and propane (Kondratenko et al., 2006), and epoxidation of allylic alcohols. However, the activity of VPO catalysts in liquid phase reactions is very limited. To the best of our knowledge, the application of vanadium-based catalyst in the synthesis of polyhydroquinolines has not been reported, although there have been reports on the application of vanadium-based catalysts in organic synthesis such as tetrahydropyranylation of alcohols, thiols, and phenols (Choudary et al., 2001), acylation of alcohols and phenols (Oskooie et al., 2008), dihydropyrimidin-(2*H*)-ones (Sabitha et al., 2003b), and coumarins (Sunil Kumar et al., 2006).

The present study details a highly efficient route for the synthesis of polyhydroquinolines using an inexpensive novel open-framework vanadium dodecylamino phosphate. The material was readily prepared by simple mixing of its precursors and characterised by various physicochemical techniques such as powder XRD, SEM-EDAX, FT-IR, Raman spectroscopy, UV-VIS DRS, ^{31}P and ^{13}C MAS NMR. The catalytic activity of the vanadium dodecylamino phosphate in the Hantzsch condensation synthesis of polyhydroquinolines at ambient temperature is described. The effect of various parameters such as solvent nature, catalyst dosage, and catalyst reusability was determined.

Experimental

Materials and methods

Vanadyl acetylacetonoate (Sigma–Aldrich, Bangalore, India, 98 %), dodecylamine (Sigma–Aldrich, Bangalore, India, 98 %) and orthophosphoric acid (Merck, Mumbai, India, 85 %) were used. Aldehydes were purchased from Sisco Research Laboratories, India and dimedone from Oakwood Chemical Laboratories, USA. All chemicals were of analytical reagent grade and used without further purification.

The synthesis of vanadium dodecylamino phosphate (VDDAP) was performed under ambient temperature conditions as reported elsewhere (Venkatathri et al., 2008). In a typical synthesis, a predetermined quantity of orthophosphoric acid (1 M) was added to vanadyl acetylacetonoate (0.01 M) and stirred until all the vanadyl acetylacetonoate was dissolved. Dodecylamine (4 M) was added to this well-stirred mixture and stirred well to obtain a solid product. The product thus obtained was thoroughly ground, washed with ether and dried at 50 ℃ for approximately 30 min.

Qualitative phase analysis of VDDAP was performed using a AXS D8 Advance diffractometer (Bruker, USA) at ambient temperature with CuK_α X-ray source of wavelength of 1.5406 Å using a Si (Li) PSD detector. The morphology of the synthesised material was investigated using a JSM-6390LV scanning electron microscope (JEOL, Japan) and the surface elemental composition (EDAX) was examined using a JED-2300 model (JEOL, Japan). Fourier transform infrared (FT-IR) spectra were recorded on an Avatar 370 spectrophotometer (Thermo Nicolet, UK) equipped with a pyroelectric detector (DTGS type); a resolution of 4 cm^{-1} was adopted, provided with a KBr beam-splitter. Dispersive Raman spectroscopy was performed on a Bruker Senterra at a wavelength of 532 nm using laser radiation as the source (Bruker, USA). The coordination and the oxidation state of vanadium in VDDAP were examined by diffuse reflectance UV-VIS spectrophotometry (UV-VIS DRS) on a Cary 5000 in the range of 175–800 nm (Varian, USA). Solid state ^{31}P magic angle spinning (MAS) nuclear magnetic resonance (NMR) spectra were recorded on a DRX-500 AV-III 500(S) spectrometer (Bruker, USA). The ^{31}P MAS NMR spectrum was recorded at 121.49 MHz in the frequency range of 10–12 kHz using a 5 mm dual probe head of pulse duration 5 µs. The chemical shift was measured with regard to 85 % H_3PO_4 as the external reference. The solid state ^{13}C magic angle spinning (MAS) nuclear magnetic resonance (NMR) spectra were recorded on a DSX-300 Avance-III 400(L) NMR spectrometer (Bruker, USA). The ^{13}C MAS NMR spectrum was recorded at 75.47 MHz in the frequency range of 10–12 kHz equipped with using a 5 mm dual probe head of pulse duration 4.25 µs. The ^{31}P and ^{13}C solid state MAS NMR spectra were

Table 1. Physical and spectral data of 2,7,7-trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*I*), 2,7,7-trimethyl-5-oxo-4-(4-methylphenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*II*), 2,7,7-trimethyl-5-oxo-4-(4-methoxyphenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*III*), 2,7,7-trimethyl-5-oxo-4-(4-hydroxyphenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*IV*), 2,7,7-trimethyl-5-oxo-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*V*), 2,7,7-trimethyl-5-oxo-4-(4-bromophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*VI*), 2,7,7-trimethyl-5-oxo-4-(4-nitrophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*VII*), and 2,7,7-trimethyl-5-oxo-4-(3-nitrophenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (*VIII*)

Compound	Characterisation data
I	white solid, mp/℃: 202–204 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3287, 3077, 2964, 1696, 1610 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.1 Hz, 3H), 2.13–2.32 (m, 4H), 2.37 (s, 3H), 4.05 (q, J = 7.2 Hz, 2H), 5.05 (s, 1H), 6.21 (s, 1H), 7.06–7.31 (m, 5H) MS (EI), m/z: 339 (M^+)
II	white solid, mp/℃: 260–262 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3275, 3080, 2960, 1700, 1650 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.94 (s, 3H), 1.08 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H), 2.10–2.24 (m, 4H), 2.26 (s, 3H), 2.37 (s, 3H), 4.06 (q, J = 7.1 Hz, 2H), 5.03 (s, 1H), 5.96 (s, 1H), 7.02 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H) MS (EI), m/z: 353 (M^+)
III	yellow solid, mp/℃: 255–257 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3275, 2957, 1705, 1647, 1605, 1497, 1382, 1217, 1032, 766 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.94 (s, 3H), 1.07 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H), 2.13–2.27 (m, 3H), 2.31–2.37 (m, 4H), 3.74 (s, 3H), 4.06 (q, J = 7.2 Hz, 2H), 5.00 (s, 1H), 6.01 (s, 1H), 6.72–6.75 (m, 2H), 7.20–7.26 (m, 2H) MS (EI), m/z: 369 (M^+)
IV	white solid, mp/℃: 232–234 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3390, 2955, 1700, 1645, 1590, 1480, 1385, 1220, 782 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 2.09–2.19 (m, 3H), 2.20–2.34 (m, 4H), 4.06 (q, J = 7.6 Hz, 2H), 4.98 (s, 1H), 5.61 (s, 1H), 6.10 (s, 1H), 6.65 (d, J = 8.9 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H) MS (EI), m/z: 356 (M^+)
V	off-white solid, mp/℃: 244–246 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3275, 3075, 2965, 1705, 1650, 1605 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 2.12–2.35 (m, 4H), 2.37 (m, 3H), 4.06 (q, J = 7.2 Hz, 2H), 5.02 (s, 1H), 6.13 (s, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H) MS (EI), m/z: 374 (M^+)
VI	white solid, mp/℃: 253–255 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3290, 2962, 1700, 1606, 1510, 1380, 1230, 1020, 764 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 2.19–2.27 (m, 3H), 2.34–2.41 (m, 4H), 4.05 (q, J = 7.2 Hz, 2H), 5.03 (s, 1H), 5.78 (s, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H) MS (EI), m/z: 417 (M^+)
VII	yellow solid, mp/℃: 244–246 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3288, 3077, 2964, 1705, 1605, 1530 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.93 (s, 3H), 1.07 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H), 2.12–2.41 (m, 4H), 2.12–2.32 (m, 3H), 3.99 (q, J = 7.1 Hz, 2H), 5.15 (s, 1H), 6.86 (s, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.72 (d, J = 7.9 Hz, 1H) MS (EI), m/z: 384 (M^+)
VIII	yellow solid, mp/℃: 176–179 IR (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3303, 2954, 1683, 1610, 1167, 759 ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 0.96 (s, 3H), 1.04 (s, 3H), 1.22 (t, J = 7.3 Hz, 3H), 2.10–2.34 (m, 4H), 2.38 (s, 3H), 4.01 (q, J = 7.3 Hz, 2H), 4.96 (s, 1H), 6.32 (s, 1H), 6.74–7.38 (m, 4H) MS (EI), m/z: 385 (M^+)

recorded at ambient temperature. The melting points of the polyhydroquinoline derivatives were determined using a DS-50 thermal analyser (Shimadzu, Japan). The ^{1}H NMR spectra were recorded on a AM 300 (300 MHz) (Bruker, USA) in $CDCl_3$ using TMS as internal standard. The FT-IR spectra were obtained in KBr discs on a Shimadzu spectrometer (Shimadzu, Japan). The mass spectra were determined on a Saturn 2000GC/MS instrument (Varian, USA).

General procedure for synthesis of polyhydroquinoline derivatives

A mixture of aromatic aldehyde (1.0 mmol), 5,5-dimethylcyclohexane-1,3-dione (1.0 mmol), ethyl acetoacetate (1.0 mmol), ammonium acetate (1.0 mmol), and VDDAP (0.1 g) in a methanol : water mixture ($\varphi_r = 1 : 1$) was stirred magnetically in a round-bottom flask at ambient temperature. The progress of the reaction was monitored by TLC using a chloroform : ethyl acetate mixture ($\varphi_r = 7 : 3$) as a solvent. The reaction mixture was treated with ethyl acetate (15 mL) and water (5 mL) was added to the flask. The ethyl acetate layer was separated and washed with cold water (10 mL). The organic layer was then dried over anhydrous sodium sulphate, filtered, and the solvent distilled under vacuum to afford the crude product. The crude product was further recrystallised from absolute alcohol to afford the pure product. The structures of the products were confirmed by physical and spectroscopic data (IR, ^{1}H NMR, and MS spectra) as compared with the data in the literature. The spectral data of some polyhydroquinoline derivatives are given in Table 1.

Results and discussion

Catalyst characterisation

The powder X-ray diffraction pattern (Fig. 1) of VDDAP shows peaks at 2θ of 5.5°, 8.1°, 10.8°, 13.5°, 21.2°, 22.2° and the corresponding d-spacings are 15.9 Å, 10.8 Å, 8.1 Å, 6.5 Å, 4.1 Å, 3.9 Å. The peaks at 2θ of 21.2°, 13.5°, and 22.2° indicate the presence of vanadium ions (Xue et al., 2010) of $VOPO_4$ phases (Rownaghi et al., 2009), and hydrated $VOPO_4$ phases ($VOHPO_4 \cdot H_2O$) predominantly in the V^{4+} state with a small amount of V^{5+} species in VDDAP (Guan et al., 2008). The crystallite size of the VDDAP was calculated by employing Scherer's equation

$$D = \frac{0.9\lambda}{\beta \cos\theta} \quad (1)$$

where D represents the mean grain size, λ is the wavelength of X-ray radiation, β is the full width at half the maximum height of the peak, and θ represents the diffraction angle. The average crystallite size of VDDAP was found to be 2.09 nm.

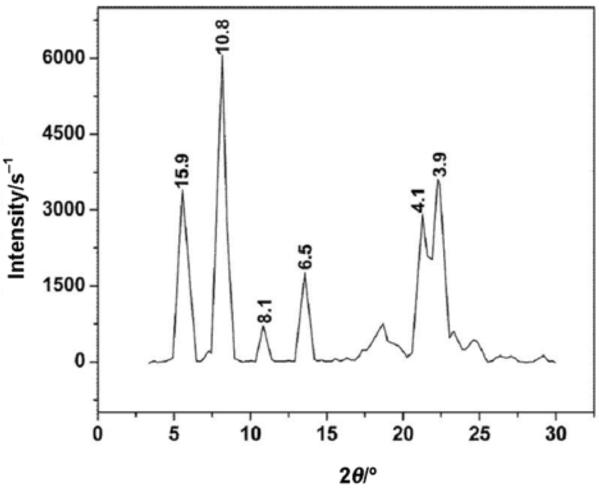


Fig. 1. PowderX-ray diffraction pattern of VDDAP.

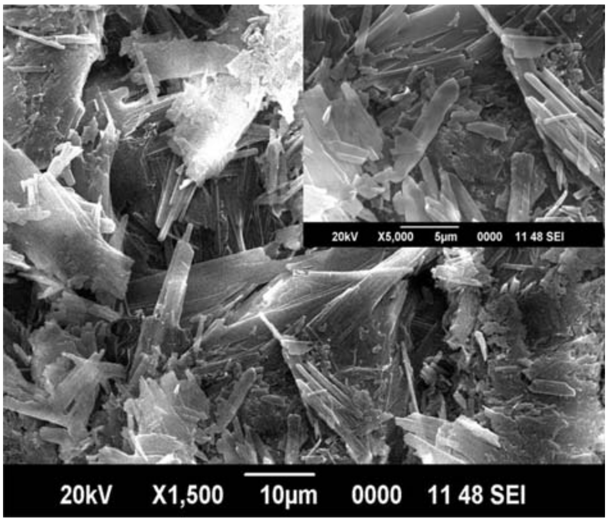


Fig. 2. Scanning electron micrograph of VDDAP (inset shows high resolution image of VDDAP).

The scanning electron micrograph (Fig. 2) shows that the particles have a fibrous morphology (Machado et al., 2004). The energy dispersive X-ray analysis (Fig. 3) shows the distribution of the constituent elements O, P, N, and V in the synthesised material (Table 2).

The Fourier transform infrared spectrum (Fig. 4) of VDDAP shows a peak at 540 cm^{-1} associated with the V—O—V rotational vibrations. The small edge at 2920 cm^{-1} and the peak at 1475 cm^{-1} correspond to the asymmetric stretching and bending vibrations of methylene groups ($-CH_2$) of amine. The peak at approximately 1220–1080 cm^{-1} corresponds to the C—N stretching vibration. The peaks at 1085 cm^{-1} and 1171 cm^{-1} are due to the asymmetric stretching and anti-symmetric stretching of the P—O bond, respectively (Borah & Datta, 2010). The band at

Table 2. Elemental analysis of VDDAP

Element	Atomic number	Series	Content		Error
			mass %	at. %	%
O	8	K-series	56.54	58.86	32.2
P	15	K-series	19.07	10.25	0.8
N	7	K-series	14.02	16.67	5.8
C	6	K-series	10.21	14.16	4.2
V	23	K-series	0.16	0.05	0.0
Total			100.00	100.00	–

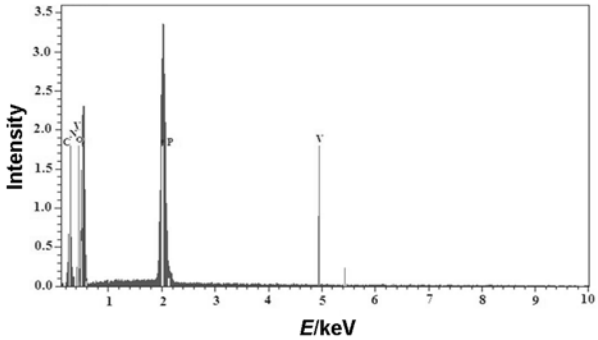


Fig. 3. Energy dispersive X-ray analysis spectrum of VDDAP.

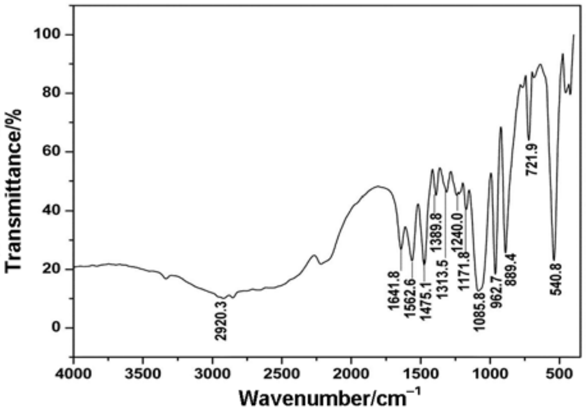


Fig. 4. Fourier transform infrared spectrum of VDDAP.

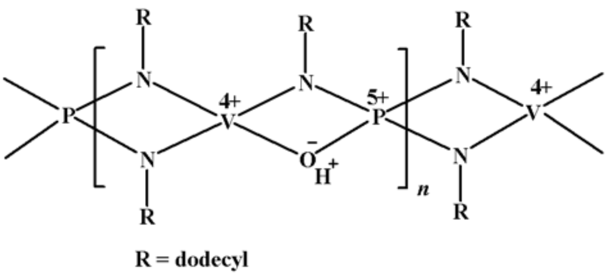


Fig. 5. Structure proposed for VDDAP.

1240 cm^{-1} can be ascribed to the asymmetric stretching vibration mode of the P—O bond (Nagaraju et al., 2008). The peaks in the range of 850–980 cm^{-1} are attributed to the stretching frequency of the –V═O bond in VDDAP (Nguyen-Phan et al., 2011). The peak at 889 cm^{-1} may correspond to the presence of condensed P—N units in VDDAP. The absence of bands at 1580 cm^{-1} and 1540 cm^{-1}, which are characteristic of the N—H bending vibrations of the NH_3^+ group, indicates that the incorporated amine is not in the protonated form (Datta et al., 2005). Absorption band corresponding to the $VOPO_4$ lattice vibration at 962 cm^{-1} was retained after the synthesis, suggesting the lamellar nature of the compound involving a V—P—O framework with the organic molecules. The structure of VDDAP was found to possess vanadium phosphate layers in which the amine molecules interact with the vanadium and phosphate to form an open-framework sandwiched polymeric material (Fig. 5).

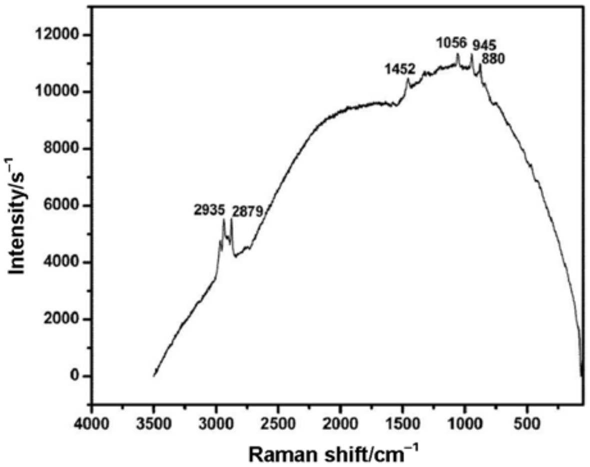


Fig. 6. Dispersive Raman spectrum of VDDAP.

The dispersive Raman spectrum (Fig. 6) of VDDAP shows a small peak at 880 cm^{-1} corresponding to the presence of $VOHPO_4 \cdot H_2O$ (Guliants et al., 1996) while the band at 1050 cm^{-1} is assigned to the strong V—O—P band of the $VOPO_4$ phase in VDDAP (Wu et al., 2010). The band near to 945 cm^{-1} corresponds to the symmetric stretching vibration of the phosphate tetrahedron of the $VOPO_4$ phase in VDDAP (Beneš et al., 2006).

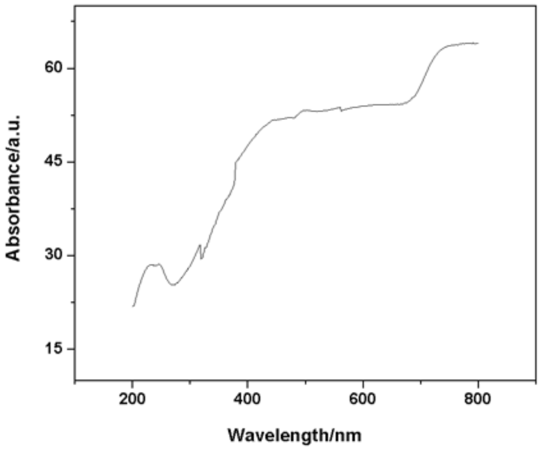


Fig. 7. UV-VIS diffuse reflectance spectrum of VDDAP.

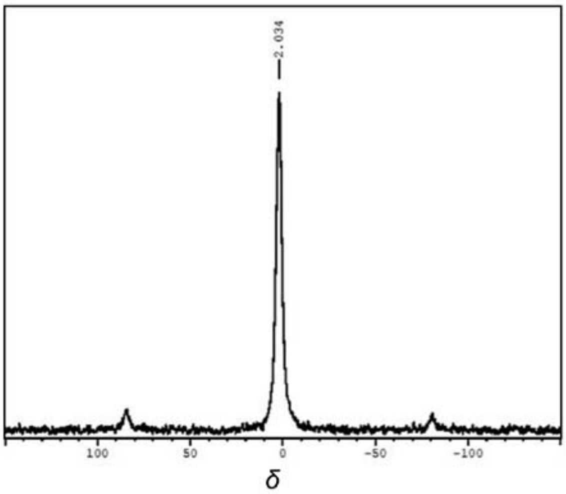


Fig. 8. ^{31}P MAS NMR spectrum of VDDAP.

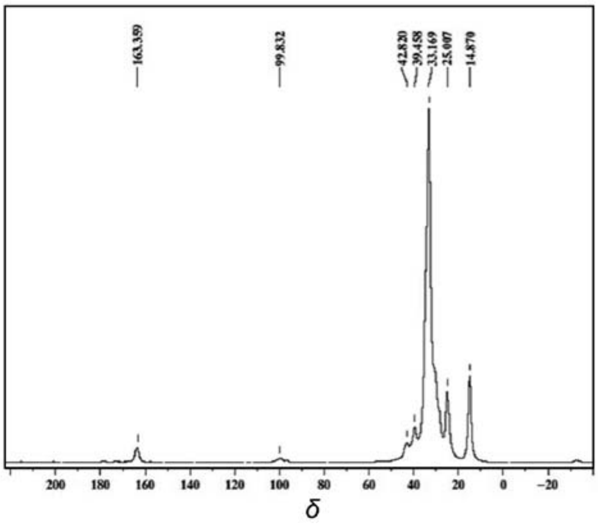


Fig. 9. ^{13}C MAS NMR spectrum of VDDAP.

The UV-VIS diffuse reflectance spectrum (Fig. 7) of VDDAP shows a band at 250 nm due to the VO^{2+} species present in the tetrahedral coordination. The band at 300–320 nm favours high dispersion of V^{5+} ions in the tetrahedral environment (Wang et al., 2011). The UV-VIS diffuse reflectance spectrum indicates that V^{4+} and V^{5+} ions are coexistent in the catalyst. The presence of a broad peak at 410–460 nm is due to the charge transfer transitions of the V^{5+} species (V=O) in square pyramidal geometry.

The solid state ^{31}P MAS NMR spectrum (Fig. 8) of VDDAP shows a sharp signal centred at $\delta = 2.034$. The signal corresponds to the phosphorous atoms of the phosphate linkage. The ^{31}P MAS NMR signals in the δ range from –22 to 4 correspond to the phosphorous atoms of the $VOPO_4$ phases. That only one resonance peak present is a clear indicator that all the phosphorous atoms are equal in VDDAP.

The ^{13}C MAS NMR spectrum (Fig. 9) of VDDAP shows that the ^{13}C chemical shift in the δ range of 32–34 is due to the alkyl chains of interior methylene carbons in trans conformation (Dasgupta et al., 2002). The peak at $\delta = 14$ is due to the interaction of the terminal methyl group of dodecylamine with the VPO matrix. The peaks at $\delta = 42.8$ and $\delta = 39.4$ correspond to the carbon (C_1) adjacent to the amine head group and the carbon (C_2) next to it, respectively, indicating the strong interaction of the amine head group with the vanadium phosphate matrix (Dasgupta et al., 2004).

Catalytic studies

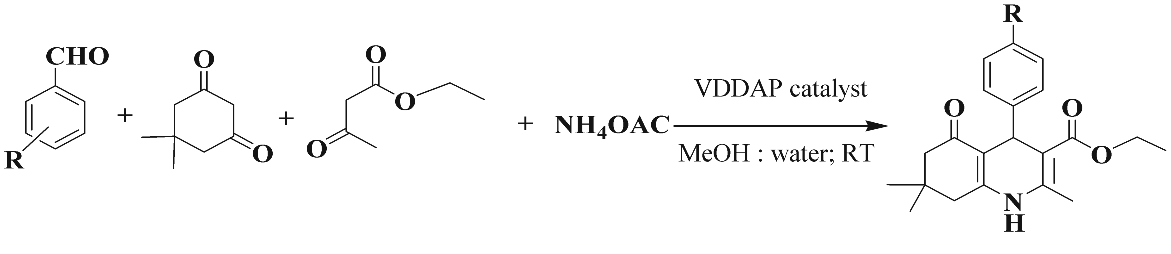
The applicability of a novel VDDAP in the synthesis of polyhydroquinolines is reported for the first time.To explore the efficacy of the catalyst and the optimum conditions required for the reaction, the four component condensation of benzaldehyde (1.0 mmol), 5,5-dimethylcyclohexane-1,3-dione (1.0 mmol), ethyl acetoacetate (1.0 mmol), and ammonium acetate (1.0 mmol) in a solvent-free media and without any catalyst were investigated at ambient temperature. It was found that under these conditions a very low yield was obtained. The same reaction was performed in the presence of VDDAP under solvent-free conditions and the time required for the reaction to achieve a slight yield was 240 min.

Since the solvent properties play a crucial role in organic reactions, the effect of various solvents differing in polarity was studied on the synthesis. Solvents such as ethanol, acetonitrile, chloroform, methanol, aqueous methanol solution, water, and tetrahydrofuran were screened using the model reaction. Acetonitrile, chloroform, water, tetrahydrofuran, and the solvent-free system did not favour formation of product. Ultimately, the methanol or methanol : water ($\varphi_r = 1 : 1$) mixture was found to be a solvent sys-

Table 3. Reaction of benzaldehyde, ethylacetoacetate, dimedone, and ammonium acetate in the presence of 0.1 g of catalyst VDDAP at ambient temperature: effect of solvents

Entry	Solvent (5 mL)	Time/min	Yield^a/%
1	Methanol	140	75
2	Ethanol	180	65
3	Acetonitrile	NR	–
4	Chloroform	NR	–
5	Tetrahydrofuran	NR	–
6	Methanol : water (1 : 1)	120	83
7	Water	NR	–
8	Solvent-free	240	63

a) Isolated yield; NR – no reaction.



I–VIII

Fig. 10. VDDAP catalyst-mediated synthesis of polyhydroquinolines.

Table 4. Reaction of benzaldehyde, ethylacetoacetate, dimedone, and ammonium acetate in methanol : water (1 : 1) mixture at ambient temperature: effect of VDDAP catalyst dosage

Amount of catalyst/g	Time/min	Yield^a/%
0.03	290	59
0.05	220	68
0.07	180	74
0.10	120	85

a) Isolated yield.

tem permitting the reaction to proceed smoothly but yielding a moderate amount of the product (65 %). When VDDAP was used in the presence of the methanol : water ($\varphi_r = 1 : 1$) mixture at ambient temperature the reaction was completed smoothly within 2 h and afforded the product with an 83 % yield (Table 3, entry 6). The results indicate that polar solvents, methanol, and water, solubilise the reactants, bring the reactants onto the surface of the catalyst and enhance the yield. Studies show that VDDAP in the presence of the methanol : water mixture was found to be an effective catalyst towards the reaction in respect of reaction time as well as of the product yield at ambient temperature (Fig. 10).

To study the optimisation of the catalyst, the reaction was investigated using different amounts of catalyst ranging from 0.03 g to 0.1 g (Table 4). It was found that the reaction product yield increased with the increase in the amount of catalyst. The reaction yield was found to be 85 % for 0.1 g of catalyst whereas it was 68 % for 0.05 g of the catalyst. The results indicate that an increase in the amount of VDDAP significantly improved the reaction; this may be due to presence of vanadium ions. The optimum amount of catalyst was found to be 0.1 g with regard to product yield. The role of the catalyst is to activate the aldehyde by binding the oxygen atom of the aldehyde with the vacant orbital of vanadium in VDDAP (Fig. 11).

Fig. 11 shows a tentatively proposed mechanism for the synthesis of polyhydroquinolines. The synthesis of polyhydroquinolines follows the Knoevenagel reaction between ethyl acetoacetate, benzaldehyde, and ammonia to afford their condensation and ester enamine intermediates, respectively. Further, dimedone undergoes Knoevenagel condensation with ammonia and benzaldehyde to give ester enamine and cyclic benzaldehyde derivatives of dimedone. The intermediates thus formed further undergo condensation to yield polyhydroquinolines.

Subsequent to the above results, the protocol was extended to a variety of aromatic aldehydes using VDDAP (0.1 g) in the methanol : water ($\varphi_r = 1 : 1$) mixture at ambient temperature. The effect of aromatic aldehydes carrying either electron-donating or electron-withdrawing substituents in the *ortho*, *meta*, and *para* positions exhibits equal facility in product formation with good to high yields. But the *para*-substituted aldehydes afforded better results than the *ortho* substituent due to the steric hindrance asso-

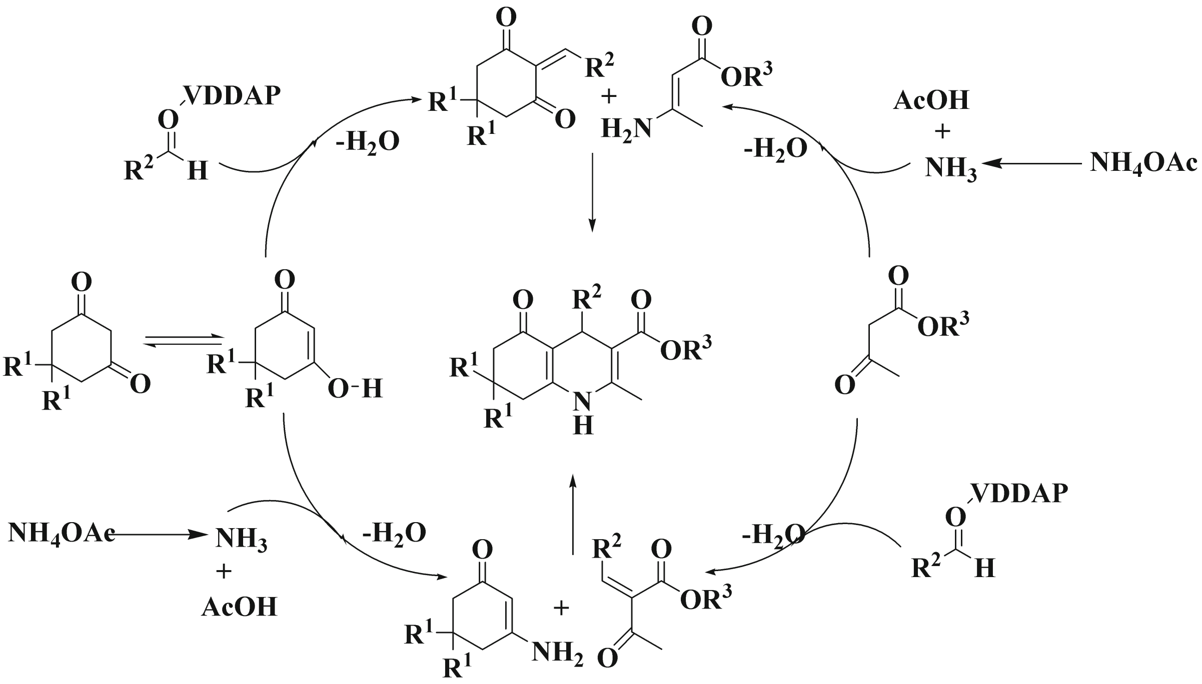


Fig. 11. Proposed reaction mechanism for formation of polyhydroquinolines.

Table 5. VDDAP catalysed (0.1 g) synthesis of polyhydroquinoline derivatives in methanol : water (1 : 1) mixture at ambient temperature: effect of substituents

Entry	Ar	Time/min	Yield[a]/%
1	C_6H_5	120	83
2	p-ClC_6H_5	135	70
3	p-MeC_6H_5	140	68
4	p-$OMeC_6H_5$	160	69
5	m-$NO_2C_6H_5$	120	78
6	p-OHC_6H_5	90	73
7	p-FC_6H_5	120	76
8	o-$NO_2C_6H_5$	110	79
9	p-$NO_2C_6H_5$	90	82
10	p-BrC_6H_5	90	80

a) Isolated yield.

Table 6. Reusability of VDDAP catalyst for synthesis of polyhydroquinolines using methanol : water (1 : 1) mixture

Entry	Run	Time/min	Yield/%
1	Fresh catalyst	120	83
2	1	180	79
3	2	200	75
4	3	230	74

ciated with the *ortho* substituent. The corresponding products and yields are presented in Table 5. It was also observed that aldehydes bearing electron-withdrawing groups facilitated the reaction rapidly and afforded higher yields in shorter reaction times.

The catalyst reusability was examined by treating benzaldehyde (1.0 mmol) 5,5-dimethylcyclohexane-1,3-dione (1.0 mmol), ethylacetoacetate (1.0 mmol), and ammonium acetate (1.0 mmol) in the presence of VDDAP (0.1 g). At the end of the reaction, the catalyst was removed by filtration, washed with diethyl ether, dried at ambient temperature, and re-used in the succeeding cycles. The reaction proceeded smoothly with an increase in reaction time and afforded moderate to good yields in successive runs. The results show that the catalyst could be re-used for three successive runs without appreciable loss of catalytic activity. The product yields achieved in the subsequent cycles were found to be 83 %, 79 %, 75 %, and 74 % (Table 6).

Conclusions

In summary, a novel VDDAP was synthesised at ambient temperature employing a vanadium precursor in the presence of phosphate using organic amine as the template. The powder XRD data suggest the presence of $VOPO_4$ and hydrated $VOPO_4$ phases in the framework of the material. The presence of –V=O and V—O—P bonds in the framework was confirmed by the presence of the corresponding vibrational bands of the infrared and Raman spectra. The coexistence of V^{4+} and V^{5+} in the framework was suggested from the UV-VIS DRS studies. The ^{31}P MAS NMR spectrum revealed the phosphorous atoms to be of the $VOPO_4$ phases. ^{13}C suggests the interaction of an amino group with the vanadium phosphate matrix. The catalytic application of this material in the synthesis of polyhydroquinolines demonstrated the efficiency of the material. The use of this inexpensive and reusable catalyst renders the protocol attractive from an economic perspective. The catalyst can be recycled and reused without any loss of catalytic activity in subsequent cycles of the reaction. These characteristics render the procedure an attractive alternative to the existing methods for the synthesis of polyhydroquinolines at ambient temperature in a one-pot synthesis.

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