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Vitamin B_1 supported on silica-encapsulated γ-Fe_2O_3 nanoparticles: design, characterization and application as a greener biocatalyst for highly efficient acylation

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A new magnetic catalyst was synthesized by the immobilization of vitamin B_1 (thiamine hydrochloride) on the surface of silica-encapsulated γ-Fe_2O_3 nanoparticles. Its capability was evaluated in the acylation of alcohols and phenols with acetic anhydride under solvent-free conditions and afforded the desired products in high yield. This novel magnetic organocatalyst could be separated from the reaction vessel by use of an external magnet and recovered 5 times without a significant loss of its activity. The amount of loaded vitamin B_1 on the silica-encapsulated γ-Fe_2O_3 was assigned by TGA and confirmed by back titration. Availability, cheapness and low toxicity are reasons associated with the utilization of vitamin B_1 as a catalyst. The catalyst has been characterized by FT-IR, XRD, SEM, VSM and TG/DTA.

Introduction

Thiamine hydrochloride (vitamin B_1) named as the "thio-vitamin" is a water-soluble vitamin found in the vitamin B complex. Vitamin B_1 (VB_1) consists of pyrimidine and thiazole rings linked by a methylene bridge (Fig. 1). The use of VB_1 analogs as powerful catalysts for various organic transformations has been reported.[1]

Vitamin B_1 is an essential cofactor in all living systems where it functions to stabilize the acyl carbanion synthon[2] and catalyzes the nonenzymic decarboxylation of pyruvate to α-acetolactate and acetoin in mildly basic aqueous solutions.[3] In the 1960's, Ronald Breslow, proposed that vitamin B_1 could be used as a catalyst in biochemical acyloin condensations and serves as a coenzyme for three important types of transformations (a) nonoxidative decarboxylations of α-keto acids (b) oxidative decarboxylations of α-keto acids (c) formation of acyloins.[4] Magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3), are two main illustrative examples of MNPs, and are noteworthy in regard to the medical and pharmaceutical fields, due to their biocompatibility and biodegradability.[5]

Recently, appreciable attempts have been devoted towards the development of magnetic nanoparticles (MNPs) and upgrading their applicability in many diverse areas. The accurate surface functionalization of MNPs is critical because it controls their physicochemical effects, colloidal suspension steadiness and biological fate.[6] The fixation of active biomolecules *via* covalent attachment to a silica surface for biotechnological processes is a remarkable synthetic approach.[7]

In order to reduce the problems of using mineral acid catalysts (*e.g.* H_2SO_4 and HCl) and solid acid catalysts such as clays, zeolites, sulfated metal oxides and heteropolyacids,[8] we are interested in the design of 'greener' heterogeneous catalysts. So we envisioned a novel renewable and environmentally safe Brønsted acid catalyst (vitamin B_1 supported on a magnetic surface). After characterization of the catalyst, its activity was evaluated for the acylation of alcohols and phenols. In the present work, to effectively utilize the catalytic properties of VB_1, we have developed an efficient procedure to tether VB_1 on a magnetic surface.

Fig. 1 Structure of Vitamin B1 (VB1).

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Results and discussion

Synthetic *Modus Operandi* and characterization of γ-Fe_2O_3@SiO_2 coated with vitamin B_1

FT-IR spectra. FT-IR appears to be the best technique to confirm the modification of Fe_2O_3@SiO_2. To evaluate the best possible conditions for the loading of vitamin B_1 on silica, multifarious solvents and bases were investigated. The FT-IR

peaks of the nanoparticles did not change in the absence of a base, which means that vitamin B_1 was not attached on the silica. Our results confirmed that, by adding base, the silica is capable of covalently binding to vitamin B_1. In this study, various solvents were tested under basic conditions to investigate the effect of solvent on the enhancement of vitamin B_1 loading. The FT-IR peaks clearly changed in the presence of triethylamine with methanol as the solvent. Then the reaction was done at different temperatures. The FT-IR peaks of the system exhibited distinguishable changes in the presence of triethylamine as the base in methanol at 80 °C. We propose that the ammonium salt produced from the reaction of triethylamine and vitamin B_1 catalyzed the formation of covalent binding between silica and thiamine. Substitution includes the O nucleophile of silica attacking the electrophilic C in the hydroxyethyl side chains of thiamine displacing a water molecule.

FT-IR spectra of Fe_2O_3@SiO_2, vitamin B_1, Fe_2O_3@SiO_2@thiamine and Fe_2O_3@SiO_2@vitamin B_1 are depicted in Fig. 2. The spectrum of Fe_2O_3@SiO_2 (a), shows a band around 461 cm^{-1} which can be attributed to the stretching vibrations of the Fe–O bond in the γ-phase Fe_2O_3. Also, the bands around 804 and the strong band at 1089 cm^{-1}, are associated to vibrations of the symmetric stretching of Si–O–Si and asymmetric of Si–O–Si, respectively in the spectrum of Fe_2O_3@SiO_2 confirming that silica is well coated on the γ-phase Fe_2O_3. The spectrum of supported γ-Fe_2O_3@SiO_2 with thiamine (c) also shows small bands around 2900 cm^{-1} that are related to asymmetric and symmetric C–H stretching. The signals located at 3416 cm^{-1} can be attributed to the N–H stretching and confirmed that thiamine was tethered on a silica surface through its hydroxyl group. In the spectrum (c) for thiamine functionalized γ-Fe_2O_3@SiO_2, the peak at 1626 cm^{-1} can be ascribed to the C=N or C=C bands stretching frequency. The spectrum of the supported γ-Fe_2O_3@SiO_2 with vitamin B_1 revealed an asymmetric and symmetric C–H band stretching frequency at around 2900 cm^{-1} and the N–H stretching frequency was shifted to a higher wavelength at 3430 cm^{-1} and its intensity decreased indicating that NH_2 had been converted to its chloride salt in the last step. Also, the broad peak of the hydroxyl group hasn't been observed in this spectrum confirming hydroxyl groups are linked to silica surface (d).

Scanning electron microscopy (SEM). The morphology of nano γ-Fe_2O_3@SiO_2@vitamin B_1 was evaluated using scanning electron microscopy (SEM). The SEM image of the supported catalyst showed uneven-sized particles due to deposition of the silica on magnetic nanoparticles (Fig. 3).

X-ray diffraction (XRD). Average size was calculated by using Scherrer's formula $D = 0.9\lambda/\beta \cos\theta$ to be about 80 nm, D is the average crystalline size, λ is the X-ray wavelength ($\alpha = 1.78897$ Å), β is the angular line width of half-maximum intensity and θ is Bragg's angle in degrees (Fig. 4). Diffraction peaks at around 35.5°, 43.1°, 54°, 62.8°, corresponding to the (311), (400), (440) and (511) are identified from the XRD pattern. It is apparent that the diffraction peaks of our magnetic silica nanoparticles match to the standard pattern for crystalline maghemite (γ-Fe_2O_3) with an inverse spinel structure[9] and also confirming that the nanoparticles are coated with silica.

Vibrating sample magnetometry (VSM). The magnetic possession of the γ-Fe_2O_3@SiO_2@vitamin B_1 was measured by vibrating sample magnetometry (VSM). Magnetization (emu g^{-1}) as a function of applied field (Oe) is depicted in Fig. 5 with the confined field from −10 000 to 10 000 Oe.

Bare nanocrystals of γ-Fe_2O_3 have a high saturation magnetization of 68 emu g^{-1} at room temperature[10] which decreased to 15 emu g^{-1} for γ-Fe_2O_3@SiO_2@vitamin B_1, nonetheless it is enough to remove this catalyst from the reaction vessel with an ordinary magnet.

VSM shows the hysteresis loops of the γ-Fe_2O_3@SiO_2@vitamin B_1 at room temperature. The zero remanence and coercivity of magnetization curve demonstrate that these silica nanoparticles have super paramagnetic properties. With the γ-Fe_2O_3@SiO_2@vitamin B_1 dispersed in CH_2Cl_2 an external magnetic field can easily gather the nanoparticles in less than one minute (Fig. 6), and then with a slight shake they can promptly be re-dispersed, the results show that the particles display good magnetic characteristics and that they can be applied as a magnetic catalyst.

Thermo-gravimetric analysis (TGA) and differential thermal analysis (DTA). Piccaluga and co-workers have reported DTA measurements of γ-Fe_2O_3@SiO_2 (ref. 11) that showed an endothermic peak at a low temperature (lower than 200 °C) due to water elimination and exothermic signal over 600 °C.

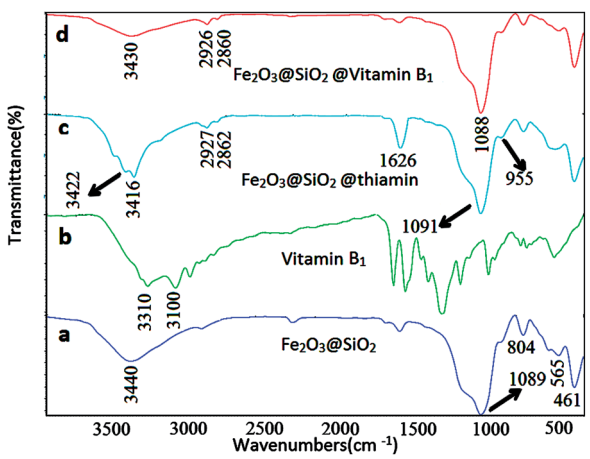


Fig. 2 FT-IR spectra of γ-Fe_2O_3@SiO_2 coated with vitamin B_1.

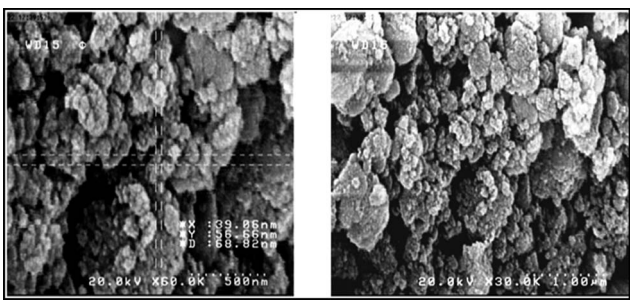


Fig. 3 SEM analysis of the γ-Fe_2O_3@SiO_2@vitamin B_1.

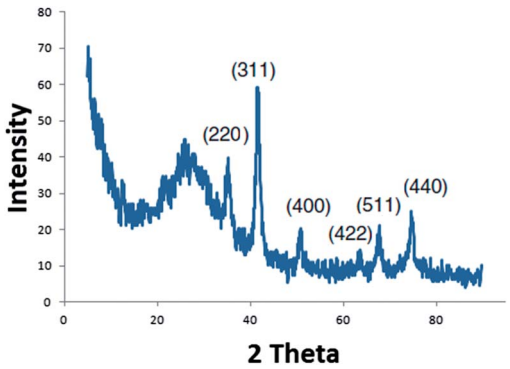


Fig. 4 The X-ray diffraction patterns of the γ-Fe_2O_3@SiO_2@vitamin B_1.

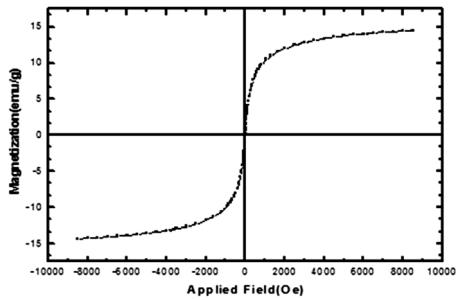


Fig. 5 Magnetization curve of γ-Fe_2O_3@SiO_2@vitamin B_1.

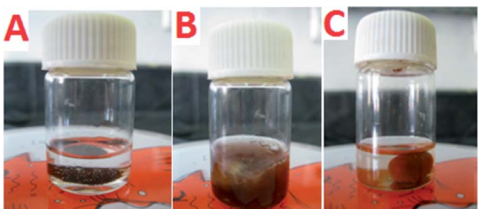


Fig. 6 Visualization of the γ-Fe_2O_3@SiO_2@vitamin B_1 collection process using a magnetic bar: (A) before the reaction without a magnet bar (B) during stirring with a magnet bar (C) collection on the magnet bar after reaction.

Thermogravimetric analysis (TGA/DTA) of γ-Fe_2O_3@SiO_2 coated with vitamin B_1 is depicted in Fig. 7.

The endothermic peak below 200 °C showed a weight loss of this catalyst of 5% that can be assigned to the release of physisorbed molecules on the surface of γ-Fe_2O_3@SiO_2. There are two exothermic peaks accompanied with a mass loss of 5.5% in the temperature range of 200–600 °C in the DTA curve of γ-Fe_2O_3@SiO_2 coated with vitamin B_1. These peaks were mainly attributed to the decomposition of organic groups grafted to the γ-Fe_2O_3@SiO_2 surface. The peak higher than 600 °C most probably corresponds to a phase transition in which the amorphous phase is converted to a crystalline phase.[11] In this temperature range, XRD shows the starting point of the α-Fe_2O_3 formation. Also the transition γ- to α-Fe_2O_3 gives an exothermic DTA trace,[12] that in the present case, is superimposed on the amorphous to γ-Fe_2O_3 transition trace.

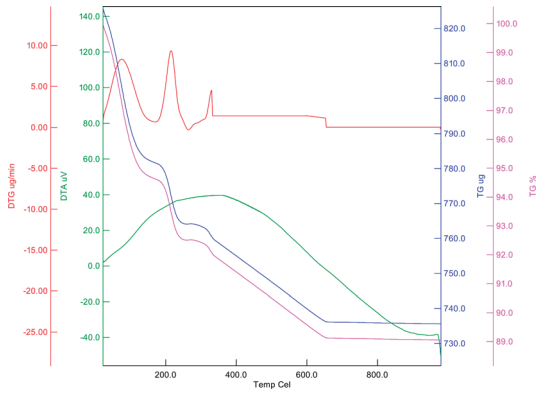


Fig. 7 Thermogravimetric and differential thermogravimetric of γ-Fe_2O_3@SiO_2 coated with vitamin B_1.

Through the TGA analysis, the vitamin B_1 content of γ-Fe_2O_3@SiO_2 was evaluated to be 0.2 mmol g^{-1}.

The acidity of vitamin B_1 loaded on the silica-encapsulated γ-Fe_2O_3 was confirmed by the back-titration method. Thus, triplicate ~100 mg samples, were added to 5 mL of 0.1 N NaOH solution. To ensure that all of the vitamin B_1 was reacted with NaOH, an excess amount of NaOH was used. The mixture was sonicated for 10 minutes. To each vessel, was added two drops of phenolphthalein pH-indicator. Back-titration was accomplished by titrating the unreacted base in solution with standardized 0.1 N HCl solutions to the first permanent cloudy pink colour. This was subtracted from the primary amount of base to find the amount of base that actually reacted with the vitamin B_1 as an acid and hence the quantity of supported vitamin B_1 on the MNPs. The acidity value was obtained as 0.2 mmol g^{-1} by adding 0.8 mL HCl.

Total number of moles of NaOH added to the sample: 0.1 mmol, total volume of HCl added to each vessel: 0.8 mL, number of moles of consumed HCl: 0.08 mmol, average number of moles of excess NaOH left after the reaction was complete: 0.02 mmol.

Thus:

$$\begin{matrix}0.02\ \text{mmol} \\ X\end{matrix} \qquad \begin{matrix}0.1\ \text{g} \\ 1\ \text{g}\end{matrix} \longrightarrow X = 0.2\ \text{mmol}$$

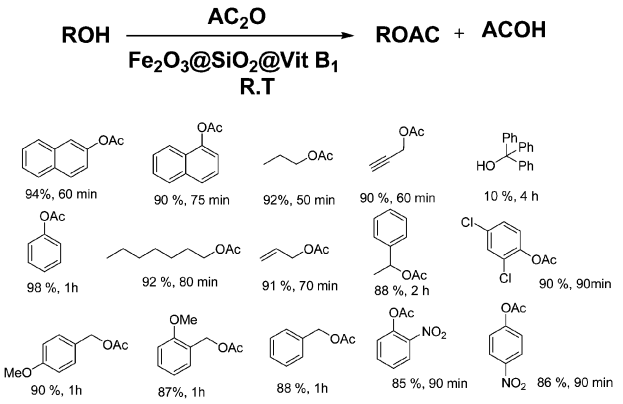
The formation of phenyl acetate from phenol was complete in the presence of vitamin B_1 (0.2 mol%) as the catalyst in less than one hour but the main problem of this reaction was the loss of catalyst at the end of the reaction.

To survey the efficacy of vitamin B_1 in this transformation, the acetylation reaction of phenol was carried out in the presence of γ-Fe_2O_3@SiO_2 which did not result in the absolute conversion of phenol to the corresponding acetate even after 2 h. This was emblematic of the necessity of vitamin B_1 in this transformation.

The acetylation of phenol in the presence of various amounts of catalyst was investigated. The conversion of phenol to phenyl acetate improved when the amount of catalyst increased from 5 mg to 10 mg however, amounts greater than 10 mg of catalyst had no significant influence in this conversion. Thus, the

optimal amount of γ-Fe_2O_3@SiO_2 coated with vitamin B_1 was 10 mg (0.2 mol%) which resulted in a 98% yield of phenyl acetate after 1 h at room temperature under solvent-free conditions. Hence, the reaction was also investigated in the presence of several organic solvents such as acetone, acetonitrile and dichloromethane as well as trying solvent-free conditions. In H_2O, the formation of phenyl acetate did not go to completion, so the optimal conditions of the reaction were selected to be without solvent, at room temperature and in the presence of 10 mg catalyst.

The supported organocatalyst was tested in the acetylation of alcohols and phenols to survey its efficacy.



Synthesis of acylated products

The reaction proceeded efficiently with high product yields and the catalyst could be recovered for at least five consecutive runs. Fig. 8 shows that the catalytic system of γ-Fe_2O_3@SiO_2 coated with vitamin B_1 worked well as phenyl acetate was produced with a high yield after the fifth run. If vitamin B_1 had been adsorbed on the surface of the silica, after the initial run this catalyst wouldn't be active in the subsequent runs. The binding between vitamin B_1 and silica should be covalent.

Experimental

All purchased solvents and chemicals were of analytical grade and used without further purification. FT-IR spectra were obtained over the region 400–4000 cm^{-1} on a NICOLET IR100 FT-IR with spectroscopic grade KBr. The powder X-ray spectrum

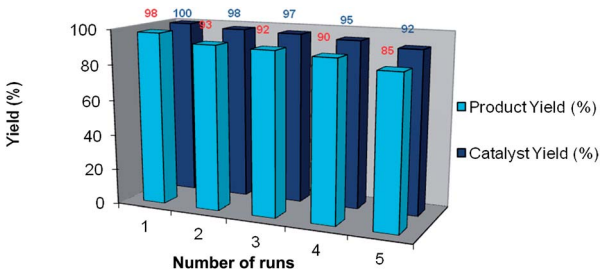
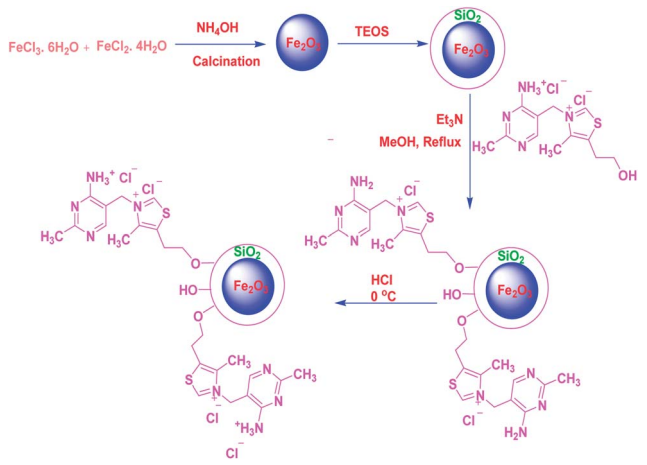


Fig. 8 Activity lost as a function of the number of reused times of the γ-Fe_2O_3@SiO_2 coated with vitamin B_1 for the synthesis of phenylacetate.



Scheme 1 Preparation of γ-Fe_2O_3@SiO_2@vitamin B_1.

was recorded at room temperature on a Philips X'pert 1710 diffractometer using Co Kα (α = 1.78897 Å) voltage: 40 kV, current: 40 mA, and the data were collected from 10° to 90° (2θ) with a scan speed of 0.02° s^{-1}. The morphology of the catalyst was studied with scanning electron microscopy using SEM (Philips XL 30 and S-4160) with gold coating equipped with energy dispersive X-ray spectroscopy. The magnetic properties of the vitamin B_1 functionalized silica-coated magnetic nanoparticles were measured with a vibrating sample magnetometer/alternating gradient force magnetometer (VSM/AGFM, MDK Co., Iran, http://www.mdk-magnetic.com). Thermogravimetric/differential thermal analyses (TG/DTA) was performed on a Thermal Analyzer with a heating rate of 20 °C min^{-1} over a temperature range of 25–1100 °C under flowing compressed N_2.

Preparation of vitamin B_1 supported on γ-Fe_2O_3@SiO_2 (Scheme 1)

(a) Preparation of Fe_3O_4 MNPs. 5 mmol $FeCl_3 \cdot 6H_2O$ and 2.5 mmol $FeCl_2 \cdot 4H_2O$ salts were dissolved in 100 mL deionized water under vigorous stirring (800 rpm) then NH_4OH solution (25%, w/w, 30 mL) was added to the above mixture at room temperature until the pH was raised to 11. The addition of NH_4OH solution followed to maintain the reaction pH between 11 and 12 at which point a black suspension was formed. The resulting black dispersion was continuously stirred for 1 h at room temperature and then refluxed for 1 h.

(b) The surface modification of γ-phase Fe_2O_3 by tetraethyl orthosilicate (TEOS). Coating of a layer of silica on the surface of the γ-Fe_2O_3 nanoparticles was achieved by adding ethanol (40 mL) to purified nanoparticles which were then heated for 1 h at 40 °C. Subsequently, tetraethyl orthosilicate (TEOS, 10 mL) was charged to the reaction vessel, and the mixture was continuously stirred for 24 h. The silica-coated nanoparticles were collected by a magnet, followed by washing five times with EtOH, diethyl ether and drying at 100 °C in vacuum for 12 h. The prepared nanoparticles at this stage are heated at 300 °C in a furnace for 3 h to convert Fe_3O_4@SiO_2 to sustainable γ-Fe_2O_3@SiO_2 nanoparticles.

(c) Preparation of γ-Fe_2O_3@SiO_2 coated with thiamine. Thiamine hydrochloride (1 mmol) was added to 1 g of the former suspension of γ-Fe_2O_3@SiO_2 nanoparticles in methanol in the presence 1.2 mmol triethylamine and refluxed for 8 h. The residue was collected by a magnet, followed by washing several times with methanol, water and ethanol to remove triethylamine and any unreacted vitamin to obtain γ-Fe_2O_3@SiO_2@thiamine.

(d) Preparation of γ-Fe_2O_3@SiO_2@vitamin B_1. To replace the acid functionality previously neutralized by triethylamine, was added 2 mL HCl (1 M) in diethylether and stirred for 3 h at 0 °C. The magnetic nanoparticles were washed with diethyl ether and distilled water, then dried for 24 h at 80 °C in an oven. The desired catalyst was formed.

Application of the catalyst in acylation of alcohols and phenols

To a stirred mixture of the alcohol or phenol (1 mmol) and $(CH_3CO)_2O$ (1.2 mmol) was added γ-Fe_2O_3@SiO_2@vitamin B_1 (10 mg = 0.2 mol%) and stirring was continued at room temperature for the appropriate time (TLC). After completion of the reaction, CH_2Cl_2 was added to the mixture to remove the catalyst by an external magnet. Water (10 mL) was added and the phases were separated. The organic phase was washed with saturated $NaHCO_3$ solution, brine, dried (Na_2SO_4) and concentrated to give the pure product. The catalyst was washed with methanol and dried to reuse. The catalyst could be recycled 5 times without a measurable loss of activity. The desired pure products were characterized by comparison of their physical data with those of known compounds.

Conclusion

In summary, vitamin B_1 was found to be a green and biocompatible organocatalyst for the acetylation of hydroxyl groups. The catalyst was easily separated from the reaction mixture by using an external magnet and thus supporting the catalyst on magnetic nanoparticles increased the efficiency of the method. Various derivatives of alcohols and phenols were converted to their corresponding acetates with high yields under solvent-free conditions. Recyclability of the catalyst was observed up to 5 times without significant loss of its catalytic activity.

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