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Enantioselective hydrogenation of 1-phenyl-propane-1,2-dione on immobilised cinchonidine Pt/SiO_2 catalysts

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ABSTRACT

Chirally modified SiO_2 containing different amounts of cinchonidine was prepared by the chemical modification of cinchonidine (CD) with trimethoxysilane over SiO_2 that had been chemically activated with 1,4-dioxane/HCl. This solid was used to support Pt catalysts containing 1 wt%Pt obtained by the chemical reduction of hexachloroplatinic acid with H_2 at 298 K and 40 bar. The materials were characterised by elemental analyses of C, H, and N, as well as thermal gravimetry (TG), DRIFT, ^{13}C NMR, ^{29}Si solid state NMR, N_2 adsorption–desorption at 77 K, X-ray diffraction (XDR), XPS, and HR-TEM. Catalytic activity for the hydrogenation of 1-phenyl-propane-1,2-dione was evaluated in a batch reactor at 298 K and 40 bar, and recycling of the catalysts yielding the largest enantiomeric excess in the products were also studied. All catalysts were found to be active in the reaction, with enantiomeric excesses of the target product (1-R-phenyl-1-hydroxy-2-propanone) ranging from 35 to 50%. The best catalyst studied was SiO_2-supported, with a nominal content of 7.5 mmolCD/L g. The recycling tests showed a loss of activity that was attributed to the surface modification of the catalyst.

1. Introduction

Catalytic enantioselective hydrogenation is one way to obtain enantiopure compounds from reducible moieties such as C=C, C=N, and C=O. For heterogeneous catalysis, supported noble metals that operate in the presence of a chiral auxiliary molecule are often used. The chiral auxiliary is generally a derivative of quinine, an alkaloid that presents three characteristic groups in its structure: a quinoline ring; an asymmetrical, bridge-type centre that incorporates a hydroxyl group; and a quinuclidine ring that can have a vinyl group ($-CH=CH_2$) on one of its vertices [1]. This inducer is generally added to the reaction system *in situ* and has been widely studied in hydrogenation reactions of α-keto esters and α-diketones [2–5]. Diverse metals such as Pt, Ir, Pd, Rh, and Ru supported on SiO_2, Al_2O_3, and others, have been used as an active phase. Cinchonidine (CD) has been the main chiral auxiliary used in hydrogenation studies of liquid phase ethyl pyruvate and 1-phenyl-propane-1,2-dione (PPD) [3,5–8].

A diverse range of improvements have been reported in the preparation of heterogeneous catalysts, including modifications of inorganic supports through the immobilisation of organometallic catalysts on SiO_2 and its derivatives [9]. Jamis et al. [10] described the encapsulation *via* sol–gel of organometallic complexes of Ru to be used in aqueous phase hydrogenations. Fan et al. proposed the use of insoluble polymers as supports for homogeneous catalysts immobilised by entrapment [11]. Complexes can also be supported through anchoring mediated by a coupling agent, typically trimethoxysilane derivatives functionalised with Cl, NH_2, or SH on materials such as Al_2O_3, La_2O_3, MCM-41, ZrO_2, TiO_2, or Fe_2O_3, among others [12–16].

The CD molecule, like organometallic complexes, can be anchored on the surface of a solid. Several authors have reported the anchoring of quinine derivatives on SiO_2 and other supports used as stationary phases in HPLC. Lämmerhofer et al. reported anchoring mediated by carbamates with the OH group at the C9 position [17], whereas Ma et al. used sulphur bridge-type bonds to immobilise quinines through the vinyl group of the quinuclidine ring [18]. Pesek et al. [21,22] studied the surface modification of SiO_2 with organic molecules, finding alkoxysilanes to be more versatile "coupling agents" (CA) for immobilising this type of substrate. The alkoxysilane was anchored by transesterification of the alkoxide groups, making the prior activation of the SiO_2 surface necessary due to the low quantity of OH groups found on the oxides typically used for catalysis and the ensuing low surface reactivity in this type of reaction [23–28]. The immobilisation of CD by means of

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the reaction between the CA and the anchored inducer have been reported [29,30] and in these studies it has been demonstrated that the presence of remaining groups of the CA on the support surface interfere in the catalytic performance [30]. If the chiral inducer is modified prior its immobilisation on the support surface it would allow a better control on the surface organic species, and therefore it is likely to assess that the anchored species correspond only to chiral inducer.

Modifications of CD were studied by the group of Toukoniitty [19,20], who introduced triethoxysilane groups into the vinyl group of the quinuclidine heterocycle and made multiple modifications to the hydroxyl group at C9 using various derivatives of chlorosilanes in enantioselective hydrogenation studies of PPD. According to those authors, modifications in the hydroxyl group heavily alter the capacity for enantioselectivity on the part of the chiral auxiliary. Thus, the inducer of chirality can be anchored on a supported metallic catalyst rather than adsorbed onto the active phase, potentially giving rise to systems reusable for consecutive batch cycles.

The presence of organic content on the surface of a support changes its thermal stability [31]. Therefore, catalysts with an immobilised organic molecule on the support must be prepared for surface metal deposition using an alternative to the traditional synthesis of supported metal catalysts (precursor impregnation, calcination, and reduction between 200 and 500 °C). Platinum has given the best results for both activity and selectivity in the hydrogenation of prochiral substrates and has been widely studied by Toukoniitty et al. [6,7,19,20,32,33]. Different physical and chemical methods have been used to prepare nanoscale Pt [34], including chemical reduction and stabilisation with polymers and oligomers [35] and electrostatic stabilisation [36], among others. For the synthesis of Pt colloids, Bönnemann and Braun [37] used formic acid as a reducing agent at 100 °C in the presence of CD as a stabilising agent. Roucoux et al. [38] assayed the activity of colloidal phases stabilised with surfactants under high pressure H_2 in the hydrogenation of α-keto esters. This methodology was used by Reyes et al. to support colloids on SiO_2, generating catalysts employed in the hydrogenation of ethyl pyruvate and PPD [39,40]. These authors found somewhat lower enantioselectivity in stabilised systems than that obtained when using an inducer adsorbed on the catalyst surface.

Our review of the literature has led us to propose the synthesis of catalysts *via* immobilisation of CD on the SiO_2 surface and dispersal of Pt over this modified support as an active phase obtained by the reduction of an inorganic precursor under high pressure H_2 during the hydrogenation of PPD under predetermined conditions.

2. Experimental

2.1. General

All air-sensitive reactions were performed in a Schlenk flask using an inert argon (Ar) atmosphere. Tetrahydrofuran (THF, Merck) was dried over metallic sodium/benzophenone; toluene (99%, Merck) was dried over metallic sodium; and triethylamine (TEA) was distilled at reduced pressure prior to use. CD (96%, Aldrich), trimethylchlorosilane (TMCS 98%, Merck), trimethoxysilane (TMS 98%, Merck), platinum cyclooctadienyl (II) chloride ($PtCODCl_2$, Aldrich), anhydrous sodium sulphate (Na_2SO_4, Merck), SiO_2 (Grace Davison), $H_2PtCl_6\cdot 6H_2O$ (40%Pt, Merck), NaOH (Merck), and other solvents (Merck) were used as received.

Elemental analyses of C, H, and N were performed on a LECO CHNS-932 analyser. TG studies were performed with a Mettler Toledo Thermogravimetric TGA/SDTA 851 using an O_2 flow of 25 mL/min and a temperature ramp of 1 K/min from 298 to 1000 K. NMR spectra for ^1H and $^{13}C\{^1H\}$ were obtained on a Bruker AMX-300 spectrometer (300 MHz for ^1H, 75 MHz for ^{13}C) using trimethylsilane as a standard; all the results obtained from the NMR of ^1H and ^{13}C were compared with the results from Toukoniitty et al. [19,20] with respect to the observed allocations and dislodged chemical signals. Solid-state ^{13}C and ^{29}Si CP NMR spectra were recorded at 100.6 MHz and 79.49 MHz, respectively, using a Bruker AV 400 WB spectrometer. Diffuse reflectance infrared Fourier transform (DRIFT) spectra were obtained using a JASCO FT/IR-6300 spectrometer. XRD patterns were recorded on a RigakuD/max-2500 diffractometer with Cu K_α radiation at 40 kV and 100 mA. N_2 adsorption-desorption analysis was performed at 77 K on a Micromeritics ASAP 2010 apparatus. Specific surface areas were determined *via* the BET (Brunauer–Emmett–Teller) equation, using adsorption data in the relative pressure range of 0.05–0.3, and pore-size distributions were estimated using the BJH model. HR-TEM micrographs were obtained with a HR-TEM Philips CM-200 system. Photoelectron spectra (XPS) were recorded using an Escalab 200 R spectrometer equipped with a hemispherical analyser and using non-monochromatic Mg $K\alpha$ X-ray radiation ($h\upsilon$ = 1253.6 eV). The surface Pt/Si and N/Si atomic ratios were estimated from the integrated intensities of Pt 4f, Si 2p, C 1s, and N 1s lines after background subtraction and correction by the atomic sensitivity factors [41]. The spectra were fitted to a combination of Gaussian–Lorentzian lines of variable proportions. The binding energy of the Si 2p peak at 103.4 eV was taken as an internal standard.

2.2. Activation of SiO_2

The surface activation of SiO_2 was performed in a round-bottom flask in which 3 g of SiO_2 was mixed with 24 mL of 1,4-dioxane and 3 mL HCl (3.1 mol/L). The mixture was stirred for 30 min at 353 K, filtered, and dried under vacuum for 4 h at 393 K.

2.3. Preparation of modified CD

The modification of CD and its subsequent hydrosilation were performed according to methods reported by Toukoniitty and coworkers [19]. An ice-cooled solution of CD (2.5 g, 8.5 mmol) in THF containing TEA (1.2 mL, 8.5 mmol) was added dropwise to TMCS (1.0 mL, 8.5 mmol). The reaction mixture was stirred for 20 h at room temperature and then for 2 h at 60 °C. The product was extracted with chloroform (50 mL) and washed with water (3× 50 mL). The water layer was extracted with additional chloroform (50 mL) and the combined organic extracts were dried over sodium sulphate. Evaporation of the solvents left 2.5 g of solid (label CD-9-O) (see Scheme 1). ^1H NMR ($CDCl_3$, δ): 8.93 (d, 1H, H-2′), 8.19 (dd, 1H, H-8′), 7.81 (br, 2H, H-5′, H-7′), 7.55 (ddd, 1H, H-6′), 7.30 (br, 1H, H-3′), 5.62 (ur, 2H, H-9, H-10), 5.07 (ur, 2H, H-11), 3.31 (ur, 1H, H-6b), 3.15 (ur, 2H, H-2a, H-8), 2.68 (ur, 1H, H-7b), 2.43 (m, 1H, H-6a), 2.11 (ur, 2H, H-2b, H-3) 1.89 (m, 1H, H-4), 1.49 (m, 1H, H-5b), 1.29 (m, 1H, H-5a), 0.85 (m, 1H, H-7a), 0.18 (s, 9H, Si–CH_3). ^{13}C NMR ($CDCl_3$, δ): 149.59 (C-2′), 148.38 (C-8a′), 146.20 (C-4′), 138.00 (C-10), 130.23 (C-8′), 129.72 (C-7′), 128.10 (C-6′), 124.72 (C-4a′), 123.52 (br, C-5′), 118.61 (br, C-3′), 116.84 (C-11), 68.74 (br, C-9), 60.84 (C-8), 56.70 (C-2), 43.06 (br, C-6), 35.49 (C-3), 29,69 (C-4), 27.12 (C-5), 18.62 (br, C-7), 0.35 (3C, Si–CH_3).

2.4. Hydrosilation of modified CD

$PtCODCl_2$ (0.018 g, 0.049 mmol) and TMS (0.77 mL, 6.0 mmol) were added at 313 K to a solution of CD-9-O (2.0 g prepared according to the previous reaction, approx. 5.5 mmol) in toluene (20 mL). The reaction mixture was stirred for 5 h at 363 K under a N_2 atmosphere. Purification by flash chromatography (hexane–acetone–TEA, 40:18:1) gave 1.25 g of the desired product as a yellowish amorphous material (TMS-CD-9-O). ^1H NMR ($CDCl_3$,