

Preparation and Characterization of Textural and Energetic Parameters of Common and Functionalized SBA-15 Mesoporous Silicas

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ABSTRACT: A set of SBA-15 ordered mesoporous silicas presenting different surface acidities was obtained by organo-functionalization. Amino and sulphonic groups were attached onto the silica surface in order to determine the influence of organo-functionalization with acidic and basic moieties on the adsorption properties of silica. Cephalexin, an antibiotic molecule characterized by its zwitterionic nature, was selected as the adsorbate. The obtained matrices were characterized by scanning electron microscopy, energy dispersive X-ray analysis and nitrogen adsorption isotherms at 77 K. Enthalpies of immersion into water, benzene and cephalexin solutions were measured by immersion calorimetry, and the cephalexin adsorption capacities of the different matrices were also determined. The structure of SBA-15 was conserved in the functionalized samples despite a noticeable reduction in the BET surface area, pore volume and pore size. It was found that the inclusion of amino groups promoted interaction between the adsorbent and adsorbate, thereby favouring the retention of cephalexin.

1. INTRODUCTION

There has been a rapid growth in the area of drug delivery over the past three decades, particularly in the search for new drug delivery systems. In recent years, many types of materials, including inorganic silica, carbon materials and layered double hydroxides (Vallet-Regi *et al.* 2001; Zhi *et al.* 2006; Vallet-Regi 2006), as well as polymeric matrices (Oh *et al.* 2008; Varshosaz 2007; Sokolsky-Papkov *et al.* 2007), have been employed as substrates for drug delivery. Amorphous colloidal and porous silicas have been proposed as drug delivery systems on the basis of silica embedding and biocompatibility (Barbe *et al.* 2004). Generally, a controlled drug delivery system can maintain the concentration of the drug in the precise site of the body within the optimum range and under the toxicity threshold, thereby improving its therapeutic effect and reducing its toxicity. In the past, controlled drug delivery was developed with polymer-based, organic systems, but novel inorganic material-based systems have also been tested more recently (Yang *et al.* 2005).

Since the discovery of ordered mesoporous silica materials in the 1990s, the synthesis and application of mesoporous solids has received great attention due to their highly ordered structures, large pore sizes and surface areas. In the past decade, a large number of applications have been established for mesoporous materials in separation and catalysis processes, and as

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sensors and devices (Taguchi and Schuth 2005; Scott *et al.* 2001). Due to their stable porous structures and well-defined surface properties, mesoporous materials seem to be ideal for the encapsulation of pharmaceutical drugs, proteins and other biogenic molecules (López *et al.* 2006, 2009a,b). In particular, it has been shown recently that SBA-15 mesoporous ordered silica may be used as a matrix for the controlled delivery of antibiotics (Muñoz *et al.* 2003; Lai *et al.* 2003; Doadrio *et al.* 2004; Lin *et al.* 2009), since it seems to possess all the required properties for use as an inorganic matrix in the controlled release of drugs, including biocompatibility (López *et al.* 2009). Additionally, previous results confirmed that modification of the silica support by changing the acidity of the SBA-15 surface contributed to achieving a controlled delivery of cephalixin monohydrate (CPX) (Legnoverde *et al.* 2009).

In the present work, amino- and sulphonic-modified SBA-15 mesoporous silicas have been prepared and the tailored materials used as adsorbents for the antibiotic cephalixin. Attempts have been made to obtain a greater insight into the nature of the change in the adsorption forces generated by acidic or basic groups anchored onto the surface by combining techniques such as titrations and adsorption capacity with the enthalpies of immersion of the modified silicas into an aqueous solution of CPX and water. These enthalpies corresponded to the respective interactions between the acidic and basic groups present on the silica surface and amino and carboxylic groups present in the antibiotic, and to their enthalpy of hydration when all other conditions were maintained constant.

Direct post-functionalization using sulphonic groups was not possible and the best results for drug adsorption were obtained using post-amino-functionalized samples. Our objective was to synthesize SBA-15 materials having surface groups of different acidity in order to evaluate the influence of the surface acidity on the adsorption enthalpies and drug adsorption. The results obtained enable this influence to be accounted for, since it has been shown that, despite its highest BET area, the adsorption of drugs by common SBA-15 is not particularly high. The improvement in drug adsorption produced by the presence of basic surface groups has been demonstrated conclusively.

2. EXPERIMENTAL

2.1. Chemicals

The chemicals used in this study included the triblock copolymer poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide) (Pluronic P123; M.W., 5800; Aldrich, St. Louis, MO, U.S.A.), tetraethyl orthosilicate (TEOS, 98%, Aldrich), hydrochloric acid (Merck), 3-aminopropyltriethoxysilane (APTES, Aldrich), 1,4-dioxane (Carlo Erba), 3-mercaptopropyltrimethoxysilane (MPTMS; Alfa Aesar, Ward Hill, MA, U.S.A.), hydrogen peroxide (H₂O₂, Panreac, Spain), sulphuric acid (J.T. Baker) and cephalixin monohydrate (CPX, Interlude Company S.A.).

2.2. Synthesis of materials

A sample of SBA-15 (SBA-15_{CO}) was prepared according to the methodology described by Zhao *et al.* (1998). Thus, 4 g of Pluronic P123 block copolymer was dissolved in a 2 M aqueous HCl solution. The temperature of the solution was increased to 35 °C and TEOS added dropwise to the system under vigorous stirring for 5 min. The stirring rate was decreased and maintained at this value for 20 h. After this time, the reaction mixture was heated to 80 °C for 24 h. The resulting

white precipitate was separated from the liquid phase by filtration and further washed with de-ionized water. Finally, the polymer was removed by calcination in air at 540 °C for 6 h. The nominal molar composition for the final product was 0.041TEOS:6.67H₂O:0.24HCl:0.0007P123.

The amino-functionalized sample was obtained by post-synthesis treatment. To anchor the amino groups to the SBA-15 surface, the calcined sample was refluxed for 16 h in a 6.66 v/v% solution of 3-aminopropyltriethoxysilane in 1,4-dioxane. The resulting solid was recovered by filtration, washed with the solvent and dried (40 °C, in vacuum) to constant weight (Nguyen *et al.* 2008). This solid is denoted below as SBA_{FA}. For the synthesis of SBA-15 containing sulphonic groups, the mesoporous silica material was firstly functionalized with mercaptopropyl groups using the sol-gel technique. The synthesis procedure involved co-hydrolysis of TEOS with MPTMS in the presence of P123 as the templating agent in aqueous HCl. After thiol functionalization, the resulting solid was oxidized by soaking in an aqueous solution of hydrogen peroxide (H₂O₂, 30 vol%) following the method described by Margolese *et al.* (2000). To eliminate any triblock copolymer situated inside the pores, the solid obtained was washed with ethanol, followed by filtration. The resulting powder was then dried for 2 h at 120 °C. This sample is denoted below as SBA_{FS}.

2.3. Characterization

The synthesized solid samples were analyzed by different techniques. Scanning electron micrographs were obtained using a Philips 505 scanning electron microscope, while semi-quantitative chemical analyses aimed at estimating the S/Si and N/Si ratios were performed by energy dispersive X-ray analysis (EDX) using a DXPRIME 10 attachment to the scanning electron microscope. Transmission electron microscopy (TEM) was carried out employing a JEOL 1200EX II instrument using an acceleration voltage of 100 kV. Nitrogen adsorption/desorption isotherms were measured at -196 °C using a Micromeritics ASAP 2020 instrument (Micromeritics Corp., Atlanta, GA, U.S.A.). The surface area was determined by applying the BET equation, while the pore-size distribution was obtained from the desorption branch of a given isotherm using the Barrett-Joyner-Halenda (BJH) method. Before adsorption, samples were outgassed by heating at 100 °C at pressures less than 3×10^{-2} mmHg for 12 h.

The change in acidity due to functionalization was determined by potentiometric titration. Thus, a known mass of the solid to be analyzed was suspended in acetonitrile and the suspension titrated using a 0.1 N solution of n-butylamine in acetonitrile at a dropping rate of 0.05 ml/min. The variation in the electrode potential was recorded on a digital pH meter (Metrohm 794 Basic Titrimetric apparatus with a double junction electrode). Additionally, the enthalpies of immersion of the three different silicas into benzene ($-\Delta H_{\text{Imm}}$, C₆H₆), water ($-\Delta H_{\text{Imm}}$, H₂O) and 10 mg/ml CPX aqueous solution ($-\Delta H_{\text{Imm}}$, CPX) were determined using a Calvet-type calorimeter (Moreno and Giraldo 2000). The $-\Delta H_{\text{Imm}}$, C₆H₆ value was used for quality control of the samples, since it is solely dependent on the structural parameters of the solid.

2.4. CPX adsorption

All the adsorption experiments were carried out at 25 °C. Adsorption isotherms of CPX onto the silica samples were obtained by dispersing the solid under stirring in a solution consisting of 10 mg/ml of CPX in water; this was checked after 20 h to ensure that liquid/solid equilibrium had been attained. After decanting and filtering, the concentration of CPX remaining in the solution was determined by UV-vis spectroscopy at 262 nm (PerkinElmer Lambda 35 instrument).

3. RESULTS AND DISCUSSION

The nitrogen adsorption isotherms obtained at $-196\text{ }^{\circ}\text{C}$ for SBA_{CO} , SBA_{FA} and SBA_{FS} (Figure 1) were of Type IV according to the IUPAC classification; these are characteristic of mesoporous solids with a narrow distribution of pore diameters. The isotherms of the three samples also exhibited type H1 hysteresis loops (López-Ramon *et al.* 1999; Leofanti *et al.* 1998). Table 1 lists the textural parameters obtained for the three samples. Silica SBA_{FA} presented a notable decrease in BET area, pore volume and pore diameter. These results are comparable with those obtained in previous work(s) (Ye *et al.* 2001; Armandi *et al.* 2008).

The data in Table 1 indicate that the surface area and pore width of the amino-modified SBA_{FA} was much smaller than for the other samples. Several authors have reported the existence of interconnection microporosity in the pore walls of SBA_{FA} , resulting in a high surface area for this material (Galarneau *et al.* 2003; Kruk *et al.* 2000). Because the co-condensation method was used to obtain the sulphonic-modified SBA_{FA} , such pores present in the sample could have been blocked by grafting SBA_{FA} with aminopropyl groups. As a consequence, the BET surface area for the amino-modified sample would be lower. The changes observed in the textural characteristics of SBA_{FA} after amino-functionalization (post-functionalization) provide evidence for the presence of functionalizing molecules attached to the pore surface. A decrease in pore size and surface area was observed when the monolayer of APTS amino groups formed on the silica surface. In contrast, in the case of sulphonic-functionalization, the synthesis method employed led to the formation of a porous structure which was practically identical with that of the non-functionalized silica. Partial replacement of TEOS by MPTS as the silica source in the formulation

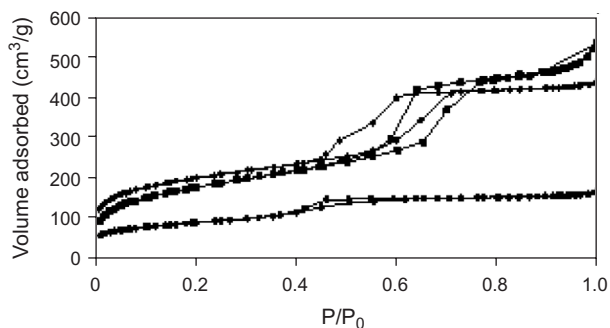


Figure 1. Nitrogen adsorption isotherms at $-196\text{ }^{\circ}\text{C}$ for (◆) SBA_{CO} , (■) SBA_{FS} and (●) SBA_{FA} .

TABLE 1. Textural Properties and CPX Adsorption Values of the Prepared Samples

Sample	BET (m^2/g)	Pore volume (cm^3/g)	Pore size (\AA)	CPX adsorption (mg/m^2)
SBA_{CO}	709	0.67	39	0.799
SBA_{FS}	631	0.80	50	0.847
SBA_{FA}	308	0.25	33	1.803

of the initial synthesis mixture, maintaining the same molar ratios for the other constituents, had virtually no influence on the textural characteristics of the synthesized solid.

The SEM images (Figure 2) show that the typical morphology of SBA-15, viz. cylinders constituted by particles with a wheat grain shape (as commonly observed in pure SBA-15 materials), was conserved after functionalization [Figures 2(b) and (c)]. This result is consistent with those obtained in similar studies (Anunziata *et al.* 2007; Sujandi *et al.* 2008) and indicates that there were no morphological differences between the obtained silicas.

Transmission electron micrographs of SBA-15 before and after functionalization are shown in Figure 3. These micrographs depict aspects of both the hexagonal arrangement of the pore channels and the silica walls. The cylindrical pores can be observed through either the top or side views; the pore mouths or tube walls can also be distinguished in this way. Their existence provides clear evidence that a hexagonal structure was maintained after functionalization.

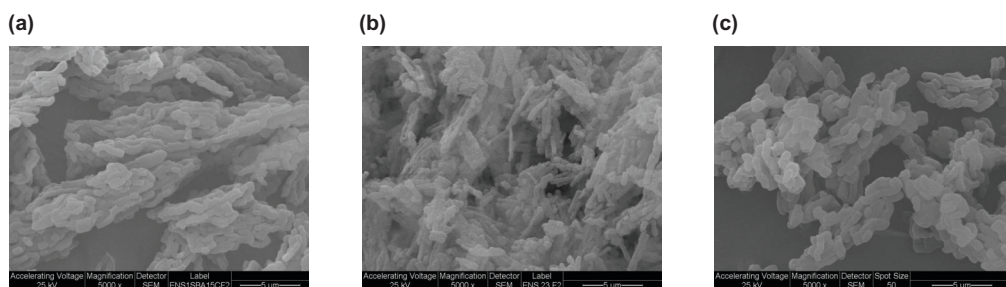


Figure 2. Scanning electron micrographs of (a) SBA-15_{CO}, (b) SBA-15_{FS} and (c) SBA-15_{FA}.

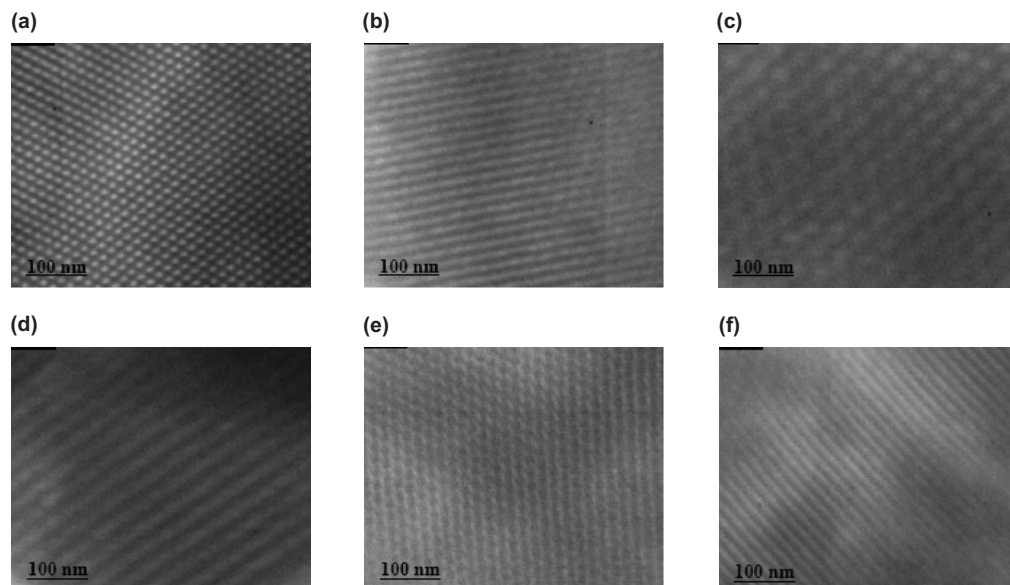


Figure 3. Transmission electron micrographs of (a,b) SBA15_{CO}, (c,d) SBA15_{FS} and (e,f) SBA15_{FA}.

Figure 4 shows the compositional analyses obtained using EDX methods. Both samples exhibited a 62% Si composition, with lower carbon and oxygen contents. Additionally, a small signal corresponding to sulphur is observed in SBA-15_{FS} [Figure 4(b)]. This signal may be related to MPTS superficial groups, suggesting the occurrence of grafting.

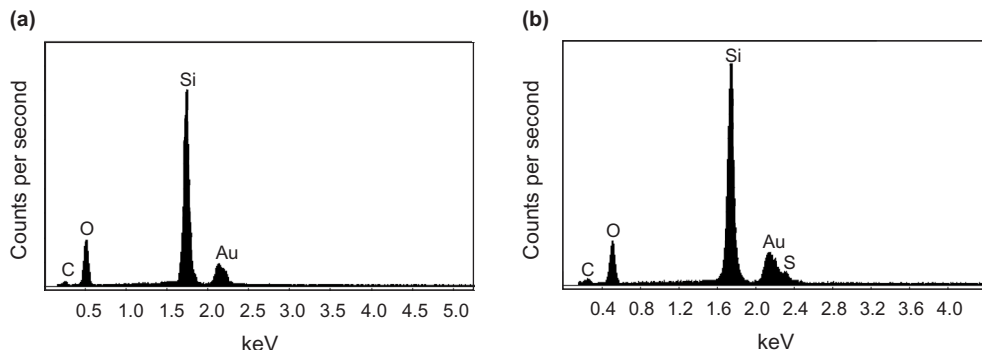


Figure 4. EDX spectra of (a) SBA-15_{CO} and (b) SBA-15_{FS}.

Potentiometric titration measurements also showed the effect of functionalization on the surface acidity. Thus, compared with SBA-15_{CO} (170 mV), both the number and strength of the acid sites increased markedly in SBA_{FS} (440 mV) but diminished in SBA_{FA} (80 mV).

Immersion calorimetry of an adsorbent into a liquid has been considered by many as a relatively simple technique for providing quantitative information about the extent, shape and chemical or physical state of the solid surface. This method also provides information on any exothermic and endothermic processes and their duration, as well as yielding enthalpy data and textural parameters that can be compared to those obtained by other techniques.

Related studies were undertaken to evaluate the surface area and pore-size distribution of the solids by reference to a non-porous carbon black, assuming that the enthalpy of immersion of the surface area was proportional to the “accessible liquid immersion area” (Denoyel *et al.* 1993). In the present work, the approximate accessible surface area (with reference to the surface area of a non-porous solid carbon black, i.e. 30 m²/g) was employed to calculate the specific enthalpy of the probe molecule using the equations:

$$-\Delta h_{\text{specific to liquid immersion}} = \frac{-\Delta H_{\text{Imm probe molecule}}}{S_{\text{carbon black}}} \quad (1)$$

$$\Delta S_{\text{accessible}} = \frac{-\Delta H_{\text{Imm probe molecule}}}{-\Delta h_{\text{specific to liquid immersion}}} \quad (2)$$

On comparing the accessible surface area obtained from equation (2) with that calculated from the nitrogen adsorption isotherms, it was found that they agreed to within 2–4%, a difference which was not considered significant for the various samples. The good correlation observed between the data is demonstrated by the plot in Figure 5. An important consideration of the model used for determining the accessible areas is that the liquid only wets the surface and does not fill the

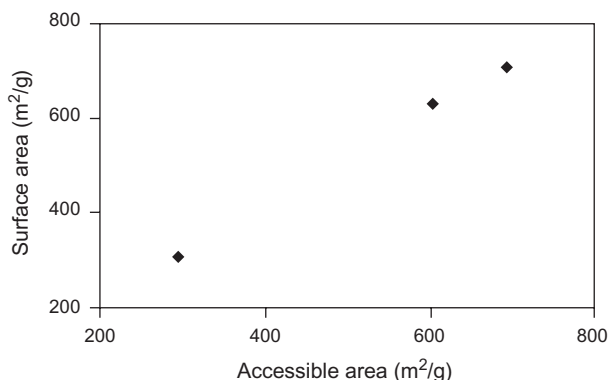


Figure 5. Relationship between the accessible area and the BET area of the silica obtained.

micropores. Since the microporous BET surface area was included in the calculation, these results demonstrate the existence of microporosity in the walls of the synthesized structures.

Figure 6 shows a comparison between the immersion calorimetric thermograms obtained for SBA-15_{CO} and SBA-15_{FA}, corresponding to the highest and lowest values for the immersion enthalpies in benzene. The first peak corresponds to contact between the solid and benzene, while the second peak corresponds to the electrical calibration. It should be noted that the magnitude of the peak for each sample was consistent with the heat of immersion obtained, being in the order SBA-15_{CO} > SBA-15_{FS} > SBA-15_{FA}. The areas beneath the respective curves also show the same relationship.

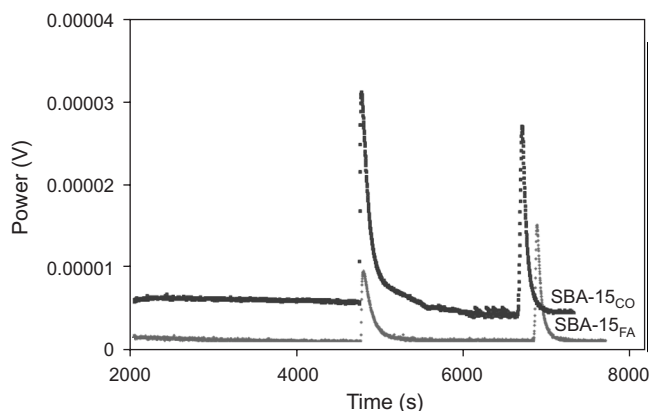


Figure 6. Benzene immersion calorimetry of SBA-15_{CO} and SBA-15_{FA}.

The values of the immersion enthalpies per unit accessible area [$-\Delta H_{\text{Imm}}$ (mJ/m²)] for the samples in water, benzene and CPX are summarized in Table 2. In all cases, the enthalpy observed between the wetting liquid and the solid was greatest for the unfunctionalized silica, while the lowest enthalpy changes occurred with silica functionalized with amino groups. This behaviour is interesting because the enthalpy data confirm the evidence provided by the nitrogen isotherms,

TABLE 2. Immersion Enthalpies of SBA-15 Silicas

Sample	Immersion enthalpy, $-\Delta H_{\text{Imm}}$ (mJ/m ²)			Accessible area (m ² /g)
	Water	Benzene	CPX	
SBA-15 _{CO}	31.0	37.4	56.0	693
SBA-15 _{FS}	18.4	30.4	35.2	603
SBA-15 _{FA}	10.9	14.4	14.3	296

viz. that the greatest influence of the amino surface group monolayer is on the textural and energetic parameters of silica.

On the other hand, Figure 7 shows the relationship between the drug adsorption abilities of the various silicas and the enthalpies of immersion in the solutions employed. In this case, the greatest drug retention occurred in the silica functionalized with amino groups. This solid also had the lowest enthalpy of contact. It would appear that the presence of amino groups on the silica surface leads to better interaction between the solid with the drug and hence a higher adsorption capacity. These results can be explained in terms of the chemical structure of CPX which exists as a zwitterion possessing both basic groups (amino) and acidic groups (carboxyl). The acid–base interactions of the different sites generate an endothermic effect that is evident in the decrease of the enthalpy of immersion obtained when the silica matrix was immersed in aqueous CPX solution.

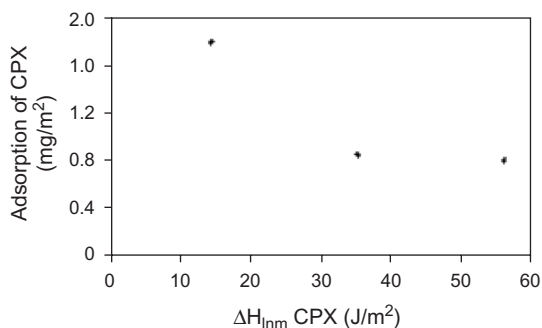


Figure 7. Relationship between the drug adsorption abilities of the various silicas studied and their corresponding enthalpies of immersion.

4. CONCLUSIONS

The experimental methodology employed allowed mesoporous silica SBA-15 and its amino- and sulphonic-functionalized derivatives to be obtained. A reduction in the immersion enthalpies and textural characteristics of the functionalized silicas was associated with the presence of surface amino and sulphonic groups. In contrast to co-functionalization, no modification of the textural parameters was observed when the post-functionalization methodology was used. An increase in the enthalpies of immersion in benzene was observed as the surface area of the immersed solid increased, and a good correlation between the surface areas determined by nitrogen adsorption and

immersion calorimetry was found. It was established that the adsorption of CPX was favoured by the presence of amino groups on the silica surface.

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