Synthesis and optimization of experimental variables of a hybrid organic–inorganic compound

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A multivariate study of the experimental parameters used in hydrothermal techniques (temperature, time, pH, relationship among reagents) was performed, and applied to the synthesis of a copper hybrid compound, $[Cu(biqui)(H_2PO_4)_2]$. In this way it was possible to rationalize the crystal yield and to find the best conditions to obtain the highest crystal production. The optimization was carried out through the Response Surface Method (RSM). The optimal values were determined over the response surface by the SIMPLEX method. These values were pH = 2.5, temperature = 123 °C, time = 3.32 days and $Cu(NO_3)_2$ mass = 0.354 g. With these values the predicted crystal mass is 0.0376 ± 0.0082 g, considering the 95% of confidence interval.

Introduction

Hybrid systems with organic and inorganic units have received considerable attention; in addition, the use of an organic moiety to build infinite metal oxides is a very important area of research in photochemistry, electromagnetism, catalysis, *etc*.[1–4] A large variety of coordination polymers has been synthesized by classical methods in solution chemistry. Nevertheless, the use of hydrothermal techniques can considerably extend the range of structural types accessible for each metal–organic system. Because of the decrease of the water dielectric constant under hydrothermal conditions, interactions between organic and inorganic partners are different from those obtained under mild conditions.[5,6]

The characteristic of hydrothermal synthesis is the use of water as a solvent in a sealed reaction container at temperatures above 100 °C. Clearly this definition can be generalized to solvothermal chemistry for the use of a sealed reaction vessel and temperatures above the boiling point of the solvent. Under these conditions, an autogeneous pressure (*i.e*. self-developing and not externally applied) is created.

There exist many works using this technique but in most of them, the chemical reaction inside the vessel is considered as a "black box".[7–10] It is possible to obtain crystalline compounds, even if the experimental parameters are not optimal. In order to obtain more crystals of better quality it is necessary to use the optimal experimental values of temperature, pH, pressure, molar relation between atoms, reaction time, *etc*. Usually it is possible to obtain more than one crystallographic phase, in a generally amorphous sample, with only few crystals; therefore, this is a severe handicap to carry out different analyses and physical measurements.

The title hybrid system comprised of copper with phosphate and biquinoline $[Cu(biqui)(H_2PO_4)_2]$, represents a paradigmatic example of this situation; Fig. 1 shows its crystal structure, as reported in ref. 11. The specimen used in the single-crystal X-ray analysis was obtained in a preliminary synthesis characterized by an extremely poor yield, in which the *ab initio* experimental parameters could only be "guessed" from previous, not always related, experiments.[11] However, the complementary analytical and magnetic studies required much larger quantities of crystalline material, a fact which prompted us to look for the optimal set of experimental parameters leading to the best possible yield. Thus, through the application of a multivariate analytical method we were able to optimize the working conditions for the synthesis, with a very interesting quantitative gain (*ca*. 50%) as compared to the original results in ref. 11.

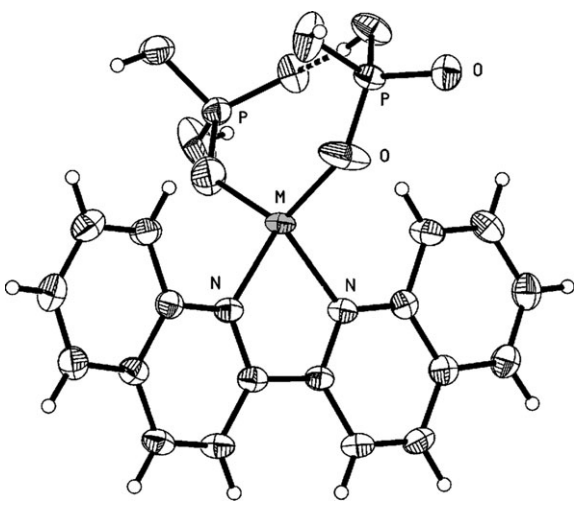

Fig. 1 Structure of $[Cu(biqui)(H_2PO_4)_2]$.

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Experimental

Synthesis and structure

Reagents were purchased from Aldrich Chemical Co. and used without further purification: $Cu(NO_3)_2 \cdot 3H_2O$, 2,2′-biquinoline and H_3PO_4 (always 5 mL) were used. The synthesis was carried out in a 23 mL poly(tetrafluoroethylene)-lined stainless steel container under autogenous pressure. The reactants were stirred briefly before heating.

The resulting solid product consisted of pale green crystals of the copper compound embedded in an amorphous phase, with a changing yield depending on the experimental variables used. The crystals were separated manually in a stereo-microscope, working under polarized light. Although it is rather easy to separate the crystalline material from the amorphous phase under these conditions, this is a slow process, and it can take several hours for each batch.

The optimal calculated conditions are $Cu(NO_3)_2 \cdot 3H_2O$, 325.4 mg, 1.55 mmol; biquinoline, 292 mg, 1 mmol; H_3PO_4 5 mL, 8.70 mmol; pH = 2.5, temperature = 123 °C and time = 3.32 days.

X-Ray characterization

The crystalline nature of the compounds obtained was confirmed in all cases by single-crystal X-ray diffraction. The samples presented, within the expected standard deviations, the same crystalline parameters and finally, the same structure (triclinic, $P\bar{1}$, a = 7.809(2), b = 10.522(2), c = 12.362(2) Å, α = 91.79(1), β = 91.72(1), γ = 106.63(1)°).

Structure

Fig. 1 show the structure of the compound, with the copper cation chelated by a biquinoline unit through its two N atoms, and two monocoordinated phosphates completing the distorted tetrahedral environment.

The phosphate anions coordinate through one of their unprotonated O, the remaining one being an acceptor of an intramolecular H-bond linking both phosphate moieties into some sort of a single unit. The interaction of this O seems to be strong enough as to weaken its bond to P; in fact, $P{=}O_{uncoord}$ are longer than $P{=}O_{coord}$ in all four independent moieties.

The two-dimensional structure presents the biquinoline groups protruding outwards (both sides), in such a way as to interdigitate when planes stack along b. The interaction between adjacent planes is achieved through π–π contacts involving aromatic rings in neighbouring biquinoline groups. The details of this structure can be found in ref. 11.

Multivariate analyses

In order to determine the conditions to obtain a maximum amount of crystals, the following reaction parameters were optimized: pH (X_1), temperature (X_2), time (X_3), and $Cu(NO_3)_2$ (X_4). The optimization was carried out through the Response Surface Methodology (RSM).[12–15] The aim of this analysis is to create a quadratic polynomial function. A central composite circumscribed design is used, made of a factorial design and star points.[16] The variable values are coded and normalized to unitary values, −1 and +1. For X_1 the values ranged from 2.00 to 3.00, for X_2 they ranged from 110 to 130 °C, X_3 from 2.00 to 4.00 days and for X_4 they ranged from 0.121 to 0.482 g. In these ranges, the central point (coded 0) was set at 2.50 for X_1, 120 °C for X_2, 3.00 days for X_3 and 0.241 g for X_4, being determined in triplicate to variance determinations. The star points were distributed at a distance of $n^{1/2}$ from the central point, where n is the number of variables (4). The star points ranged from 1.50 to 3.50 for X_1, 100 to 140 °C for X_2, 1.00 to 5.00 days for X_3 and from 0 to 0.664 for X_4. The response factor was the crystal mass obtained (Y).

A second-order function describing the system's behavior was determined by a Multiple Linear Regression (MLR). The statistical validation was performed by an ANOVA test with at 95% confidence level. The optimal conditions values were determined over the response surface by the SIMPLEX method.[16] All the calculations were carried out using the Modde 7.0 software.

Discussion

From the results of the multivariate analyses a polynomial response to crystal amount was obtained for the analyzed variables, eqn (1), which considers the relative importance of the different terms. The coefficients were normalized according to codified variable values. In this polynomial the errors are the confidence intervals at 95%. (The first term of the polynomial is a constant, therefore is not represented in the graph; after it, the terms are correlated with the graph.)

$$Y\,(\%) = 3.81\ (\pm 0.47) - 0.178X_1\ (\pm 0.153) + 0.328X_2\ (\pm 0.153) + 0.387X_3\ (\pm 0.153) + 0.373X_4\ (\pm 0.191) - 0.633X_1^2\ (\pm 0.164) - 0.607X_2^2\ (\pm 0.164) - 0.617X_3^2\ (\pm 0.164) - 0.371X_4^2\ (\pm 0.167) \quad (1)$$

In order to highlight the importance of each variable, their coefficients in the polynomial were plotted (Fig. 2).

Considering the first-order coefficients of each variable, it can be concluded that there are no significant differences between the variables, since their confidence intervals overlap. This positive coefficient implies that there is a positive dependence of crystal amount with the increase of these variable values. The negative second order coefficients indicate a maximum region described by a parabola. There were not

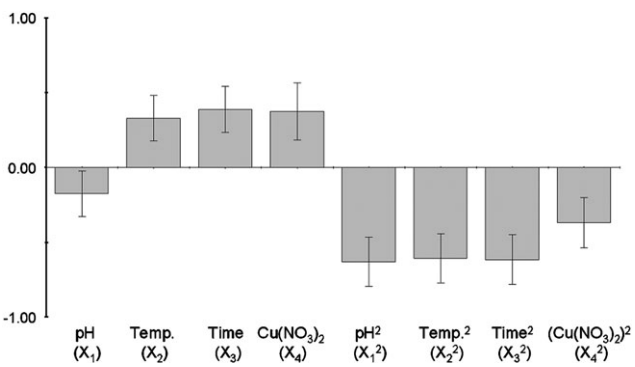

Fig. 2 First- and second-order coefficients plot from the polynomial response. The error bars are at 95% confidence intervals.

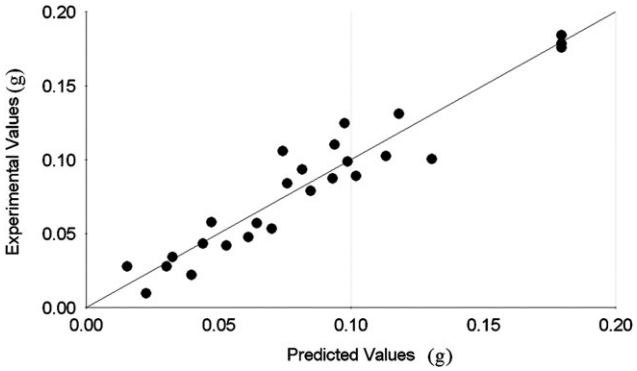

Fig. 3 Calculated and experimental results for crystal amount.

any significant correlations between variables, and so they could be considered independent.

The polynomial model was validated through an ANOVA test with 95% confidence level.

We compared the experimental results obtained from the experimental design with the predicted response by the polynomial (Fig. 3). No significant difference between the calculated and the experimental values was observed, with a linear regression value $R^2 = 0.914$. This indicates a validated prediction from the response polynomial.

In Fig. 4 and 5 the surface plots of the polynomial response are shown. In these graphs two variables are plotted, keeping constant the other two at optimized values. The regions of maximal crystal mass are shown by a circular layer >0.0350 g. Fig. 4 shows the crystal mass as a function of the $Cu(NO_3)_2$ mass (X_4) and pH (X_1): a maximum region can be observed at $Cu(NO_3)_2$ mass in the range 0.265–0.447 and pH 2.20–2.66. The crystal mass as a function of temperature (X_2) and time (X_3) is shown in Fig. 5. There is a maximum with time varying from 2.80 to 3.83 days and temperature (X_2) ranging from 117 to 128 °C.

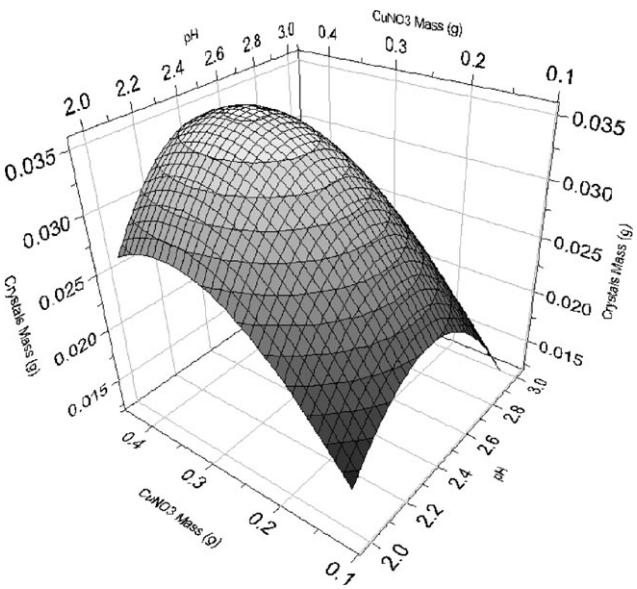

Fig. 4 Response surfaces for the crystal mass obtained as a function of pH and Cu(II) concentration ratio.

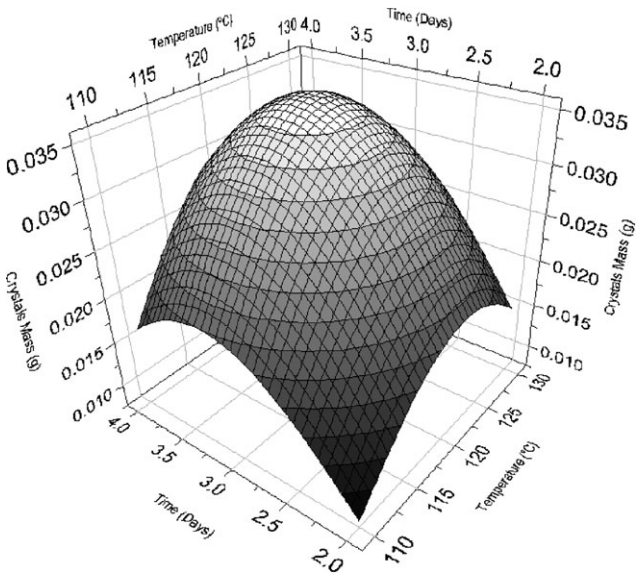

Fig. 5 Response surfaces for the crystal mass obtained as a function of temperature and reaction time.

Through SIMPLEX analysis over the response surface the optimal values for crystal mass were achieved. These were: pH = 2.5, temperature = 123 °C, time = 3.32 days and $Cu(NO_3)_2$ mass = 0.354. With these values the predicted crystal mass from the polynomial is 0.0376 ± 0.0082 g, considering the 95% confidence interval, reflecting an experimental mean value of 0.0314 g.

Conclusions

The analytical method, RSM, is valid to optimize the experimental conditions in the hydrothermal synthesis of the $[Cu(biqui)(H_2PO_4)_2]$ system. The theoretical crystal yield is in agreement with experimental values.

Acknowledgements

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