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Application of Chemometrics to Heterogeneous Catalysis: Optimization of 1,4-Cyclooctadiene Yield and Selectivity in the Isomerization of 1,5-Cyclooctadiene Catalyzed by Silica-Supported $Ir_4(CO)_{12}$

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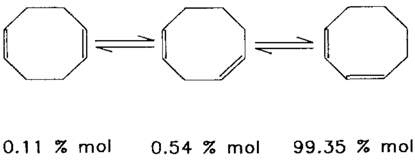
The isomerization of 1,5-cyclooctadiene to 1,3-cyclooctadiene and 1,4-cyclooctadiene catalyzed by silica-supported $Ir_4(CO)_{12}$ was investigated by means of statistical methods, and the yield in 1,4-cyclooctadiene was optimized. A complete factorial design was developed in order to evaluate the effects of five experimental variables and their interactions. Response surface methodology was employed to study the experimental domain (level of variables) and to determine the values of the independent variables for which the responses assume optimum values. By this method optimum yield in 1,4-isomer (50%) was obtained with the highest selectivity (>97%) so far obtained in this reaction.

INTRODUCTION

It has recently been reported that 1,4-cyclooctadiene (1,4-COD) can be successfully used as a starting material in the copolymerization reaction with 1,5-cyclooctadiene (1,5-COD) using Calderon-type catalysts (*1*). The low availability of 1,4-COD (via organic synthesis) (*2*) has until now limited its use in these reactions. Since 1,5-COD is largely available as a by-product of the cyclotrimerization of butadiene, it is a good starting material for obtaining 1,4-COD by catalytic isomerization:



SCHEME 1

The percentages indicate the equilibrium composition of the mixture at 100°C (*3*), which shows that only a kinetically controlled process, possibly operating under continuous conditions (*1*), would enable one to obtain 1,4-COD in high yields.

We have previously reported that Group 8 and 9 metal clusters supported on silica effectively catalyze the isomerization of 1,5-COD to 1,4- and 1,3-isomers, under both flow and batch conditions (*4, 5*). In particular, $Ir_4(CO)_{12}$ turned out to be the most promising metal cluster, since good yield (60%) and good selectivity (80%) in the 1,4-COD isomer were obtained (*5*). However, the reaction mixture contained up to 15% of 1,3-COD, which makes the separation of the desired product difficult (*1*). With the purpose of improving both yield and selectivity and keeping as low as possible the content of 1,3-COD, a systematic study of this system has been undertaken.

Since adjustments of "one-variable-at-a-time" (OVAT) often fail in attempting optimization (*6*), multivariate methods, which are mathematical and statistical techniques

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which allow one to scan efficiently and rationally the experimental domain (*7*), have been adopted. With this approach, the optimization is reached with fewer experiments since all variables are changed simultaneously and studied at various levels.

STATISTICAL METHODS

In any synthesis a large number of experimental variables will influence the chemical result. Hence, some kind of dependence between the result y and the experimental factors $(x_1 \ldots x_n)$ can be assumed and it can be approximated by a Taylor expansion, i.e., a polynomial in the experimental variables:

$$y = b_0 + \Sigma_i b_i x_i + \Sigma_i b_{ii} x_i^2 + \Sigma_{i<j} b_{ij} x_i x_j + \Sigma_i b_{iii} x_i^3 + \ldots . \quad (1)$$

This polynomial can be used to explore the response surface, that is the graphical representation of a relationship between a system response and one or more quantitative variables (*6*).

Often only a few of the variables considered will exert an appreciable influence and for screening purposes it is usually sufficient to consider linear terms and interaction terms.

Useful arrangement of the experiments required to estimate the coefficients of this polynomial equation is provided by the factorial design at two levels (*6*), which allows one to vary all factors simultaneously in a systematic way. The number of experiments to perform is *a priori* established as 2^n, where n is the number of variables considered, and must be executed in a random sequence so that the assumption of normality and independence of the experimental error is not violated.

The experimental results of a factorial design may be treated with several mathematical methods to estimate the coefficients of main effects and interactions. The significance of the coefficients may be evaluated by comparison with the standard deviation. Alternatively, the use of normal probability paper is a useful method (*6*).

When the significant variables are selected, a better approximation of the true response surface is provided by a full second-order polynomial model,

$$y = b_0 + \Sigma_i b_i x_i + \Sigma_i b_{ii} x_i^2 + \Sigma_{i<j} b_{ij} x_i x_j + e, \quad (2)$$

which is obtained by truncating the Taylor expansion after the inclusion of the second-degree terms and assuming the higher order terms to be negligible.

An appropriate set of experiments for estimating all the parameters of a full second-order model is the central composite design which is composed of a two-level factorial design plus a star design (*8*).

The interpretation of the second-order equation is not always straightforward. Canonical analysis (*6*) achieves the geometric interpretation of the response surface by a rototranslation of the axes to transform the estimated polynomial model into a simpler one. The sign and magnitude of the coefficient of the terms of the canonical equation reveal the geometric nature of the surface.

When the stationary point derived by canonical analysis is not an absolute maximum or minimum, the local extreme points can be found by constraining the independent variables one by one, two by two, etc. The Lagrange analysis of the response surface polynomial is the mathematical method used to determine these stationary points (*9*).

EXPERIMENTAL

Catalyst Preparation

$Ir_4(CO)_{12}$ was purchased from Strem Chemicals and was used without further purification. 1,5-Cyclooctadiene (EGA Chemie) was purified through a silica gel column (*10*) and stored under nitrogen over 5-Å molecular sieves. A highly porous fully hydroxylated silica (Grace Type 121, 30–50 mesh fraction, BET surface area 617 m^2/g)

was used as support. Physisorbed $Ir_4(CO)_{12}/SiO_2$ was prepared by impregnation of silica in a *n*-heptane solution of $Ir_4(CO)_{12}$ and subsequent thermal treatment at 100°C for 3 h in air. A detailed procedure for the preparation of the catalyst is reported elsewhere (*5*).

Catalytic Measurements

The catalytic experiments were carried out in a tubular stainless-steel flow reactor (14 cm length × 4.6 mm i.d.) interfaced to a gas–liquid chromatograph. 1,5-COD was vaporized into the carrier stream (argon) by means of a thermostatted saturator. In a typical run 400 mg of $Ir_4(CO)_{12}/SiO_2$ was placed in the reactor between two layers of granular quartz. The system was deaereated in flowing argon for 3 h before activation. Catalyst activation was performed at 120°C for 10 h in the presence of 1,5-COD, $P_{1,5\text{-COD}} = 48$ Torr, and argon, $P_{Ar} = 712$ Torr (1 Torr = 133.3 $N\,m^{-2}$), at a total flow of 25.4 ml/min. During this procedure, the SiO_2-supported $Ir_4(CO)_{12}$ is slowly decarbonylated and an active catalyst for isomerization of 1,5-COD is obtained (*5*). Under these conditions no effects due to diffusion as tested according to Ref. (*11*) were observed.

Calculations

Calculations for response surface were performed on an IBM PS2 Model 60 microcomputer. Response surface models were obtained by the REGFAC program package (*12*) and Lagrange analysis by CARSO program package (*9*).

RESULTS AND DISCUSSION

Screening Experiments

To take advantage of the chemometric methods which allow one to screen rapidly a large experimental domain, as many as five independent variables were investigated: x_1, reaction temperature (°C); x_2, metal loading (% wt); x_3, flow rate of 1,5-COD in the gaseous phase (ml/min); x_4, reaction time (h); x_5, partial pressure of 1,5-COD (Torr).

The choice of these variables and their values was suggested from the previous studies (*4, 5*), which showed a significant influence of the reaction temperature (x_1) on the catalyst performance. Consequently, the choice of the reaction time (x_4) as a measure of catalyst deactivation is straightforward. The -1 and $+1$ levels for these two variables were respectively 90–130°C and 3–8 h. In order to ensure that the same catalyst precursor, i.e., physisorbed $Ir_4(CO)_{12}/SiO_2$ (*5*), was always employed, the metal loading (x_2) had necessarily to be kept in a relatively narrow range (0.5 and 1.3 % wt respectively for level -1 and $+1$). The nature of the support was not considered here as a possible independent variable since it is well known that both the nature of a support and its thermal treatment can favor formation of different surface species (*13*). As far as the flow rate of 1,5-COD (x_3) and the partial pressure of 1,5-COD (x_5) are concerned, the limiting values (x_3: 0.7–16 ml_{STP}/min; x_5: 48–80 Torr) were mainly associated with physical limitations of the system employed for this study. Care was also taken to avoid any diffusional limitations. In this way the optimized reaction conditions will be obtained from the investigation of variables x_1, x_2, x_3, and x_5, while the reaction time (x_4) could account for catalyst deactivation.

The dependent responses considered at the same time were: y_1, yield of 1,3-COD (% mol); y_2, yield of 1,4-COD (% mol); y_3, amount of 1,5-COD (% mol); y_4, selectivity, [100 (% mol 1,4-COD)/(% mol 1,4-COD + % mol 1,3-COD)].

A complete factorial design 2^5 was developed. The design matrix and the experimental results are reported in Table 1 (runs 1–32). It should be noted that only 16 effective catalytic experiments were carried out since both $x_4 = -1$ and $x_4 = +1$ levels were obtained from the same run.

The coefficients of the linear polynomial were estimated by means of a table of contrasts (*6*). Such estimates are given in Table

TABLE 1

Design Matrix and Experimental Results for Each Response[a]

Run	x_1	x_2	x_3	x_4	x_5	y_1	y_2	y_3	y_4
1	−1	−1	−1	−1	−1	1.3	41.3	57.4	97.0
2	1	−1	−1	−1	−1	24.3	60.3	9.7	66.8
3	−1	1	−1	−1	−1	4.2	59.5	35.8	92.5
4	1	1	−1	−1	−1	41.1	47.1	6.9	50.6
5	−1	−1	1	−1	−1	0.9	18.4	80.7	95.4
6	1	−1	1	−1	−1	11.4	72.1	14.2	82.4
7	−1	1	1	−1	−1	3.2	34.2	62.7	91.6
8	1	1	1	−1	−1	24.5	61.7	10.3	68.8
9	−1	−1	−1	1	−1	1.3	42.7	56.0	97.1
10	1	−1	−1	1	−1	16.0	67.8	11.3	76.4
11	−1	1	−1	1	−1	4.6	62.2	32.7	92.4
12	1	1	−1	1	−1	28.8	58.2	8.7	63.8
13	−1	−1	1	1	−1	1.0	21.5	77.5	95.7
14	1	−1	1	1	−1	7.6	75.3	13.8	87.4
15	−1	1	1	1	−1	2.1	35.4	62.5	94.4
16	1	1	1	1	−1	17.4	67.2	11.6	75.9
17	−1	−1	−1	−1	1	1.7	42.4	55.5	95.2
18	1	−1	−1	−1	1	28.2	57.9	8.7	63.4
19	−1	1	−1	−1	1	2.4	52.2	45.1	95.1
20	1	1	−1	−1	1	47.3	41.6	7.2	44.8
21	−1	−1	1	−1	1	0.3	15.9	83.4	96.2
22	1	−1	1	−1	1	8.5	75.3	13.6	87.6
23	−1	1	1	−1	1	1.0	28.4	70.4	95.9
24	1	1	1	−1	1	23.5	62.2	11.2	70.1
25	−1	−1	−1	1	1	1.3	40.1	58.1	95.7
26	1	−1	−1	1	1	16.4	68.2	11.1	76.7
27	−1	1	−1	1	1	2.6	55.5	41.4	94.8
28	1	1	−1	1	1	31.8	37.7	6.2	40.2
29	−1	−1	1	1	1	0.5	16.3	83.1	96.6
30	1	−1	1	1	1	6.3	77.6	13.8	90.1
31	−1	1	1	1	1	1.0	28.2	69.6	93.1
32	1	1	1	1	1	15.6	69.1	12.5	78.9
33	−2	0	0	0	−1	0.1	5.1	94.8	97.8
34	2	0	0	0	−1	21.0	63.0	12.6	72.1
35	0	−2	0	0	−1	1.4	9.7	88.9	87.8
36	0	2	0	0	−1	12.6	64.6	21.8	82.6
37	0	0	−2	0	−1	18.4	52.6	28.2	73.3
38	0	0	2	0	−1	4.4	44.4	50.5	89.7
39	0	0	0	−2	−1	7.8	65.6	26.7	89.4
40	0	0	0	2	−1	5.7	63.5	30.8	91.8
41	0	0	0	0	−1	7.2	64.9	27.9	90.0
42	0	0	0	0	−1	7.3	65.5	25.8	88.2
43	0	0	0	0	−1	7.7	62.0	29.1	87.4

Note. Experiments 1–32: factorial design 2^5. Experiments 33–43: star design.

[a] x_1, reaction temperature (°C); x_2, metal loading (% wt); x_3, flow rate of 1,5-COD ($\mathrm{ml_{STP}}$/min); x_4, reaction time (h); x_5, $p_{1,5\text{-COD}}$ (Torr); y_1, yield of 1,3-cyclooctadiene (% mol); y_2, yield of 1,4-cyclooctadiene (% mol); y_3, amount of 1,5-cyclooctadiene (% mol); y_4, selectivity = (% mol 1,4-COD)/(% mol 1,4-COD + % mol 1,3-COD) × 100.

TABLE 2

Estimates of the Main and Interaction Effects upon the Dependent Variables

	y_1	y_2	y_3	y_4
b_0	11.82	49.80	35.71	82.58
b_1	9.98[a]	12.66[a]	−25.03[a]	−12.34[a]
b_2	3.88[a]	0.23	−4.78[a]	−4.90[a]
b_3	−4.02[a]	−2.37	7.47[a]	4.93[a]
b_4	−2.17[a]	0.43	0.46	1.74
b_5	−0.04	−1.76	1.22	−0.43
b_{12}	3.08[a]	−7.08[a]	3.43[a]	−3.71[a]
b_{13}	−3.43[a]	9.98[a]	−5.52[a]	4.98[a]
b_{14}	−2.13[a]	0.61	0.46	1.69
b_{15}	0.45	0.50	−1.36	−0.84
b_{23}	−0.64	0.65	0.45	0.98
b_{24}	−0.53	−0.41	−0.27	−0.24
b_{25}	−0.003	−1.40	0.8	−0.64
b_{34}	0.81	−0.67	−1.31	−0.24
b_{35}	−0.67	0.96	0.3	1.49
b_{45}	−0.17	−1.02	0.053	−0.63

Note. See Table 1 for meanings of symbols. The coefficients of the higher order interactions are ≤1 and are not reported here.

[a] Meaningful coefficients selected by analyzing the distribution of effects on normal probability paper.

2. The plot of these effects on normal probability paper for y_4 (Fig. 1) clearly shows that b_1, b_2, b_3, b_{12}, and b_{13} fall off the straight line that fits all the remaining effects. The same method was adopted to determine the significant effects for the other dependent variables.

The values of the coefficients reported in Table 2 deserve some discussion. Generally speaking, large values of coefficients indicate a strong influence of the variable(s) on the dependent response. In addition there is a monotonic relationship between the independent value x_i and the response y_k. Therefore, for a large positive value of b_i, on increasing the independent variable x_i a positive beneficial effect is observed for the dependent response y_k.

It appears from Table 2 that the partial pressure of 1,5-COD (x_5) has no influence on the experimental results in the range of pressure we examined. Its main effects as well as the interaction terms are indeed very small and can probably be attributed to experimental error. A slight but significant negative effect of reaction time, x_4, is found on 1,3-COD yield. This result suggests that in the experimental domain there is some catalyst deactivation, particularly at higher temperature (see b_{14} for y_1 in Table 2). Even though the influence of time is negligible for y_2-y_4, it was taken into account as a significant variable in the response surface investigation since the 1,3-COD yield is of critical importance in separation problems and in addition it may be an indication of the lifetime of the catalyst.

The temperature x_1 has the strongest influence on all the dependent responses. The value of 12.66 estimated for b_1 (Table 2) indicates that higher temperatures are needed to obtain better yield of 1,4-COD. At the same time, however, a rise in temperature causes a drop in selectivity since the estimated value of b_1 for 1,3-COD is also large and positive. Therefore, to obtain the highest yield and selectivity in 1,4-COD, a compromise solution for temperature must be selected. The interaction effects of temperature with metal loading, b_{12}, and flow

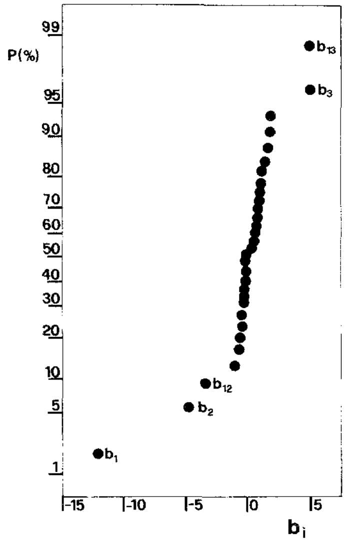

FIG. 1. Normal probability plot of estimated effects of the screening experiments for y_4.

rate, b_{13}, are always significant upon all factors, and in particular they are important for 1,4-COD yield.

Metal loading, x_2, and flow rate, x_3, are still significant from a statistical point of view, but their main effects are much less important than that of temperature. To give directions for further improvement of selectivity, metal loading should be maintained at a low level and flow rate at a high level. However, for these variables the interaction effects with temperature are comparable to the main effects, so that these interactions will constrain the search for optimum experimental conditions.

Response Surface Investigation

After the preliminary screening of the five variables, the x_5 (pressure of 1,5-COD) was discarded, because it has no influence on the dependent responses.

If a curvature is present, the screening model is not able to describe the experimental space in a suitable way. A better approximation of the true response surface is obtained by applying the full second-order polynomial model (Eq. (2)). The significance of the quadratic terms must be evaluated by means of statistical tests. Since a system of two consecutive reactions is under investigation *(14)*, a curvature should be present, at least in the 1,4-COD yield.

Although temperature, metal loading, and flow rate account for most of the variations in the experimental results, time was not discarded because of its importance in catalyst deactivation. To locate the optimum reaction conditions, response surface models of variables x_1, x_2, x_3, and x_4 were determined. For this purpose, 11 experiments were added to a 2^4 factorial design to obtain a central composite design (Table 1, runs 33–43). The former design is composed of the 16 trials of the 2^5 factorial design previously performed (Table 1, runs 1–16), in which the partial pressure of 1,5-COD, x_1, assumes its lower codified level -1 (48 Torr). The experimental data were treated by multiple regression analysis and a second-order math-

TABLE 3

Estimates of the Quadratic Model Coefficients upon the Dependent Variables and F-Test Values

	y_1	$F_{1,12}$	y_2	$F_{1,12}$	y_3	$F_{1,12}$	y_4	$F_{1,12}$
b_0	7.40		64.13		27.60		88.53	
b_1	8.10	108	12.93	46.0	−22.63	115	−9.81	109
b_2	3.52	20.5	5.66	8.83	−9.32	19.6	−3.28	12.1
b_3	−3.40	19.0	−2.90	2.32	6.64	9.98	3.66	15.1
b_4	−1.51	3.77	1.31	0.47	0.19	0.008	1.78	3.59
b_{11}	1.28	2.39	−6.61	10.7	4.89	4.81	−1.32	1.75
b_{22}	0.38	0.22	−5.83	8.32	5.30	5.66	−1.26	1.59
b_{33}	1.49	3.25	−2.99	2.19	1.30	0.34	−2.18	4.78
b_{44}	0.33	0.16	1.02	0.25	−1.35	0.36	0.09	0.008
b_{12}	2.68	7.91	−6.79	8.47	4.15	2.60	−2.48	4.61
b_{13}	−2.82	8.74	8.69	13.9	−5.51	4.58	3.68	10.2
b_{14}	−1.93	4.10	1.18	0.26	0.76	0.088	1.99	2.97
b_{23}	−0.59	0.39	−0.23	0.015	0.70	0.074	0.49	0.18
b_{24}	−0.51	0.28	0.33	0.020	0.20	0.006	0.50	0.19
b_{34}	0.52	0.30	−0.61	0.067	−0.09	0.001	−0.47	0.17
	sd = 3.82		sd = 9.34		sd = 10.30		sd = 4.61	
	$r = \pm 0.9678$		$r = \pm 0.9448$		$r = \pm 0.9654$		$r = \pm 0.9654$	

Note. Critical value of $F_{1,12}(0.05) = 6.55$. See Table 1 for meanings of symbols.

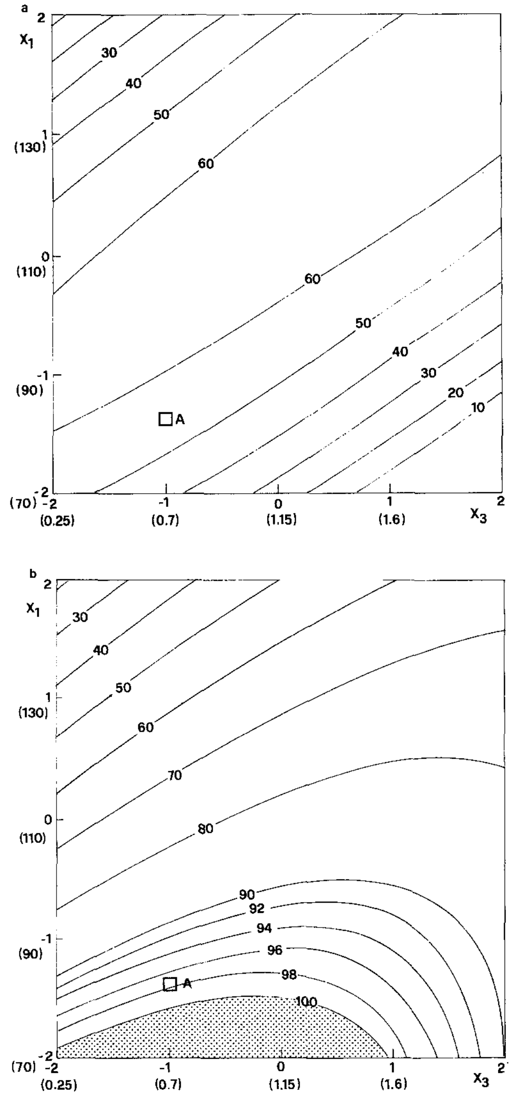

FIG. 2. Isoresponse plots obtained by REGFAC procedure from the central composite design data. (a) y_2 is the 1,4-COD yield; (b) y_4 is the selectivity. The sections were obtained under the following conditions: x_2 (metal loading) = 1 (1.3% wt); x_4 (time of reaction) = −0.6 (4 h). y-axis = x_1 (temperature); x-axis = x_3 (flow rate of 1,5-COD). A: (x_1 = −1.35; x_3 = −1).

ematical model for each response was calculated (Table 3). The estimates of coefficients of the quadratic model are in agreement with those calculated from the screening experiments. The insight on the coefficients reported in Table 3 reveals that only a limited deactivation of the catalyst with time is to be expected since all b_4 coefficients have rather small absolute values.

TABLE 4

Coefficients Calculated by Canonical Analysis for the Dependent Variables

	y_1	y_2	y_3	y_4
y_0	−0.65	62.10	13.90	98.50
L_1	3.54	1.07	7.68	1.06
L_2	0.76	0.59	4.34	−0.20
L_3	0.11	−4.96	−0.47	−1.41
L_4	−0.39	−11.10	1.39	−4.12

Note. See Table 1 for meanings of symbols.

Two quadratic terms are significant upon 1,4-COD yield (b_{11} and b_{22} in Table 3), showing that the effects of both variables are positive and follow a parabolic curve. Therefore, intermediate conditions must be searched by applying Lagrange analysis on the second-order polynomial equation.

The geometrical feature of the quadratic model was studied by means of canonical analysis. The fitted surfaces for all responses have a minimax instead of an absolute maximum, since the signs of coef-

TABLE 5

Comparison between Calculated and Observed Values in Order to Prove the Efficiency of the Response Surface

Observed	Calculated
y_1 = 1.2	y_1 = 0.83
y_2 = 55.5	y_2 = 55.5 point A in Fig. 2a
y_3 = 43.3	y_3 = 43.8
y_4 = 97.9	y_4 = 96.8 point A in Fig. 2b

Experimental values	Codified values
x_1 = 83°C	−1.35
x_2 = 1.3 % wt	+1
x_3 = 0.7 ml_{STP}/min	−1
x_4 = 4 h	−0.6

Note. See Table 1 for meanings of symbols.

ficients are not all negative (Table 4). Lagrange analysis was therefore applied to find the stationary points. After accurate screening of these points, various sets of experimental conditions corresponding to the desirable results, i.e., high yield and selectivity toward the 1,4-COD together with minimal yield of 1,3-COD, were determined. The isoresponse diagrams corresponding to one of these sets are reported in Fig. 2a for 1,4-COD yield (y_2) and in Fig. 2b for selectivity (y_4). The sections were obtained by setting x_2 (metal loading) and x_4 (reaction time) respectively at the constant codified levels of $+1$ (1.3 wt%) and -0.6 (4 h). Values higher than 50% for 1,4-COD yield are predicted for x_1 (reaction temperature) $= -1.5$, corresponding to 80°C, and x_3 (flow rate of 1,5-COD) in the range $-1.5 \leq x_3 \leq -1$ corresponding to 0.48 and 0.70 $\mathrm{ml_{STP}}$/min (Fig. 2a). Under such conditions, the selectivity is always very high (>97%) (Fig. 2b). To confirm the reliability of the model, a run was carried out under the conditions determined above. The good agreement between calculated and observed results (Table 5) confirms the efficiency of the response surface technique.

This result suggests that chemometrics can be profitably applied to investigate problems in heterogeneous catalysis.

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