JOURNAL OF CATALYSIS 137, 394–407 (1992)

Factors Influencing the K10 Montmorillonite-Catalyzed Diels–Alder Reaction between Methyl Acrylate and Cyclopentadiene

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Received July 9, 1991; revised March 25, 1992

Experimental factorial design has been used to study several factors that are assumed to affect the results of the K10-catalyzed Diels–Alder reaction between methyl acrylate and cyclopentadiene. The results obtained were complemented by physical characterization of the solid catalysts using X-ray diffraction, FTIR studies of adsorption of pyridine, methyl acrylate, and solvents, and BET measurements. Among the factors studied, the nature of the solvent is the most important one influencing the reaction results. Complementary studies have shown that solvents miscible with water give rise to low yields and endo/exo selectivities, very close to those obtained without clay in the same solvent. In these solvents the clay does not play any catalytic role and the reaction takes place in the bulk of the solvent. In general, excellent results are obtained with solvents nonmiscible with water, but a close relationship exists between the nature of the solvent and the cation exchanged into the K10 montmorillonite. In particular, anisole is the best solvent for Zn^{2+}-doped K10 montmorillonite-catalyzed reaction, but it is not so good when the exchanged cation is Fe^{3+}. In this case a radical-promoted Friedel–Crafts reaction of cyclopentadiene with anisole and oligomerization of cyclopentadiene take place. The presence of radicals has been confirmed by ESR experiments. Furthermore, in methylene chloride as solvent, catalytic activity is related to strength of Lewis acidity, and Zn^{2+}–K10 is a better catalyst than Fe^{3+}–K10.

INTRODUCTION

Smectite clays and their derivatives show catalytic activity in a wide variety of reactions. In particular, montmorillonites have been frequently used as catalysts in organic reactions involving catalysis by Brønsted or Lewis acids (*1, 2*).

The Diels–Alder reaction, leading to cyclic products with well controlled regiochemistry and stereochemistry, is a powerful tool in organic synthesis. Given the fragility and high molecular weight of the cycloadducts, the reaction usually requires the use of solvents. In the absence of catalyst several authors (*3, 4*) have shown that solvent effects are noticeable in this reaction. For instance, in the reaction between cyclopentadiene and methyl acrylate, the endo/exo selectivity is changed from 78/22 in 1,4-dioxane to 92/8 in methanol/water = 1 : 1. This solvent effect has been explained in terms of solvophobic power and polarity.

This reaction is catalyzed by Lewis acids, the use of which also increases the regioselectivity and stereoselectivity, and it has been shown that inorganic solids, such as silica gel (*5, 6*), magnesium silicate (*6*), alumina (*6, 7*), and clays(*8, 9*), can act as efficient catalysts. Laszlo *et al.* (*8*) reported that Fe^{3+}-doped K10 montmorillonite is a useful catalyst for reactions of carbonyl-containing dienophiles. In these reactions, no great influence of the solvent was ob-

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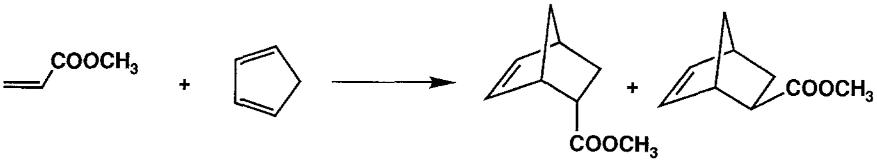

FIG. 1. Reaction between methyl acrylate and cyclopentadiene.

served on the conversion or the endo/exo selectivity when water, ethanol or methylene chloride were compared (*8*b). However, a preliminary work reported an important effect of the solvent on the reaction between cyclopentadiene and methyl acrylate catalyzed by Zn^{2+}–K10 montmorillonite (*10*). Laszlo *et al.* have also shown the importance of the nature of the cation introduced into the K10 clays. In the dimerization of dienes, in the presence of 4-tert-butyl phenol, Fe^{3+} was more active than Zn^{2+}, Co^{2+}, or Al^{3+} (*8*a). The authors suggested a radical mechanism for these reactions. As suggested by Adams (*1*), more systematic work is needed in order "*to build up the base of knowledge necessary for predictive reasoning.*"

This problem is so complex that classical analysis of this reaction would be very time-consuming, but experimental design offers an interesting alternative for the identification of experimental factors which affect catalytic activity and selectivity. Experimental design, a well known tool in several scientific and industrial areas, has seldom been used in the field of heterogeneous catalysis. This paper presents the use of experimental design for the analysis of some factors influencing clay-catalyzed reactions. In particular, the well known Diels–Alder reaction between methyl acrylate and cyclopentadiene (Fig. 1) catalyzed by K10 clays, is studied. The acidic properties of the clays can easily be monitored by cation exchange, while the size of their pores minimizes diffusional limitations of the kinetics.

TABLE 1

Metallic Ion Contents and Loss of Water in Natural and Ion-Exchanged K10 Montmorillonites[a]

	FL[b]	FL–Fe	FL–Zn	SC[b]	SC–Fe	SC–Zn
%Al	6.72	7.16	7.27	6.89	6.72	6.43
%Fe	1.81	3.75	2.24	2.12	3.95	2.32
%Zn	—	—	1.93	—	—	1.77
$\%H_2O$[c]	3.96	4.39	4.68	3.54	4.69	3.85

[a] Data referred to dry weight (120°C).
[b] FL = Fluka, SC = Süd Chemie.
[c] Weight loss at 500°C.

EXPERIMENTAL

Preparation and Characterization of the Catalysts

Cation exchange was effected by gradually adding the montmorillonite (10 g) (K10, supplied by Süd Chemie or Fluka) to stirred ferric or zinc chloride solutions (125 ml, 1 *M*) at room temperature following the procedure reported by Laszlo *et al.* (*8*d). The suspensions were stirred for 24 h, filtered, and washed chloride-free with deionised water. The resulting solids were dried overnight in a thin bed at 120°C in an oven, and ground in a mortar; the final colour of the samples is pale grey for the Zn^{2+}-clay and yellowish brown for the Fe^{3+} sample. The catalysts were equilibrated over saturated salt solutions in order to give reproducible water contents, and were analyzed by thermogravimetry in a Perkin–Elmer TGS-2 apparatus equipped with a System 4 microprocessor controller. Chemical analyses were obtained by plasma emission spectroscopy in a Perkin–Elmer Plasma 40 emission spectrometer. The results are given in Table 1.

Surface areas were calculated from BET nitrogen isotherms determined at 77 K. In all cases the values obtained fall within the range of 220–240 m^2/g. The micropore volume (pores ≤ 1 nm) is 0.1 ml/g.

X-ray diffraction patterns were recorded on a Philips computer-driven X-ray diffractometer using Cu$K\alpha$ radiation. The cation-exchanged montmorillonites retain the structure of the initial montmorillonites.

The interaction between the clays and methyl acrylate was studied by infrared spectroscopy on Nicolet 320 FT-IR and Perkin–Elmer 1600 Series FT-IR spectrometers. Acidic properties were determined by adsorption of pyridine as probe molecule on self-supported wafers. Wafers were compressed under 5 tons · cm^{-2} pressure to obtain thin disks 18 mm in diameter with a weight of ~10 mg · cm^{-2}. The resulting wafers were placed in cells (equipped with KBr windows and connected via stopcocks to a vacuum line) where the treatment of the catalysts was performed. The adsorption of methyl acrylate in the liquid phase was performed by immersion of wafers in solutions of methyl acrylate in methylene chloride and acetonitrile at the concentration used in Diels–Alder reactions and then washing with CCl_4, following the method reported by Fusi *et al.* (*11*).

ESR spectra were recorded at room temperature on a E112 Varian spectrometer working in the X band. The diphenylpicryl hydrazyl resonance line ($g = 2.0037 \pm 0.0002$) was used to measure the microwave frequency, and the magnetic fields were measured with a Bruker ERO35M nuclear magnetic resonance gaussmeter. The samples were contained in ESR 4-mm id quartz tubes.

Reaction Procedure

Methyl acrylate was purchased from Merck and used without further purification. Organic solvents were dried and purified according to standard procedures. Cycloadducts were prepared according to procedures described in the literature (*12*).

Reactions were carried out in Schlenk flasks. Preweighed (1.25 g or 2.50 g) cation-exchanged montmorillonite was dried at 120°C in an oven overnight. The flask was charged with these samples and the solvent (15 ml) under Ar atmosphere at the working temperature. Methyl acrylate (0.645 g, 7.5 mmol) and freshly distilled cyclopentadiene (0.495 g, 7.5 mmol or 1.485 g, 22.5 mmol) were added via a syringe (under these conditions a complete disolution of the reagents is achieved using any of the solvents). The reaction flask was shaken for 24 h and the reaction monitored by gas chromatography (FID from Hewlett–Packard 5890 II, cross-linked methyl silicone column 25 m × 0.2 mm × 0.33 μm, helium as carrier gas 16 psi, injector temperature 230°C, detector temperature 250°C, oven temperature program 50°C (3 min)–25°C/min–100°C (9min), retention times: methyl acrylate, 2.7 min; exo cycloadduct, 12.7 min; endo cycloadduct, 12.9 min).

Overall yields and endo/exo ratios were calculated from the solution obtained by filtration and washing of the catalyst with the reaction solvent.

Adsorption Isotherms

Preweighed clay (0.5 g) was dried at 120°C in an oven overnight. A quantity of 6 ml of a solution of methyl acrylate (or endo cycloadduct) in methylene chloride (or acetonitrile) of a given concentration (0.1, 0.3, 0.5, 0.75, 1.0, 1.5, and 2.5 *M*) were then added. The suspension was shaken for 24 h at the working temperature (20°C or −25°C); 0.1 g of *n*-decane was added as internal standard (*13*), and the solution was analyzed by gas chromatography: oven temperature program 50°C (3 min)–25°C/min–200°C (1 min), retention times: methyl acrylate, 2.7 min; *n*-decane, 7.7 min; endo cycloadduct, 8.5 min.

RESULTS AND DISCUSSION

Experimental Design

Factorial experimental design is a technique which minimizes the number of experiments needed to investigate the effect of several factors (e.g., temperature, concentration) at several levels on some measuring quantity (e.g., the yield), where results of all combinations of the factor levels are observed. The experiments are designed so as to be ideally orthogonal and approximately equally dissimilar with respect to the factors assumed to influence the measured quantity. In other words, the experiments can be represented by evenly distributed points in the corresponding factor space (*14*).

In particular, a 2^n factorial design consists of experiments with n factors at two levels. The main effect is the difference in response caused by the change in level of a factor averaged over all levels of the other factors. This has meaning in a practical sense only if the effect of a factor is not dependent on the levels of the other factors. If the effect of a factor, say A, is dependent on the level of another factor B, a second-order interaction between factors A and B is said to exist. In this case, a description of the effect of the factor A would not be complete without consideration of the interacting factor B. This concept can be easily extended to higher order interactions (*14*).

Although this methodology can be applied manually, the use of computer programs makes its application easier. We have used the NEMROD package (*15*), which easily generates complete factorial designs and their fractional replicates (see below), as well as calculating the coefficients of main effects and interactions.

Initially there were five measured quantities (responses) to be studied by means of the factorial design: the percentage of conversion after 2 h (R_1, representing the catalytic activity), the percentage of conversion after 24 h (R_2), the overall yield after 24 h after washing (R_3), the endo/exo ratio after 24 h (R_4), and the overall endo/exo ratio after 24 h after washing (R_5).

Using the same responses before and after washing permits one to test whether the adsorption of reagents and/or products introduces modifications in the behaviour of the system.

The choice of the pertinent factors determines the quality of a factorial design. Each factor must be represented by two different levels in the factorial design, so an easy experimental control of these factors is required. The first aim of these studies is to find the area of the experimental domain where the reaction takes place with good results. Therefore, when one factor plays an important role, a deeper study has to be made in order to find the physico-chemical bases of this behaviour.

TABLE 2

Factors and Levels of the Factorial Design

Factor	Level (+)	Level (−)
F_1: exchanged cation	Fe^{3+}	Zn^{2+}
F_2: clay source	Fluka	Süd Chemie
F_3: diene : dienophile ratio[a]	3 : 1	1 : 1
F_4: temperature	20°C	−25°C
F_5: solvent	CH_2Cl_2	CH_3CN
F_6: clay : dienophile ratio[b]	1 : 3	1 : 6

[a] mol : mol

[b] g:mmol.

The factors assumed to influence this reaction were chosen on the basis of prior knowledge of their influence in homogeneous or heterogeneous phases. There were six such factors, which can be divided into four categories:

—Factors affecting the catalyst: the exchanged cation (F_1) and the montmorillonite source (F_2).

—Factors affecting the reagents; the diene : dienophile ratio (F_3).

—Factors affecting the reaction conditions: the temperature (F_4) and the solvent (F_5).

—Factors affecting reagents and catalyst simultaneously: the montmorillonite: dienophile ratio (F_6).

For each factor two levels are to be chosen in order to define the factor space. These levels are given in Table 2.

Lewis acids are the most efficient catalysts for Diels–Alder reactions, so it is convenient to test clays of different Lewis acidities. Lewis acidity and the distribution between Lewis and Brønsted forms are con-

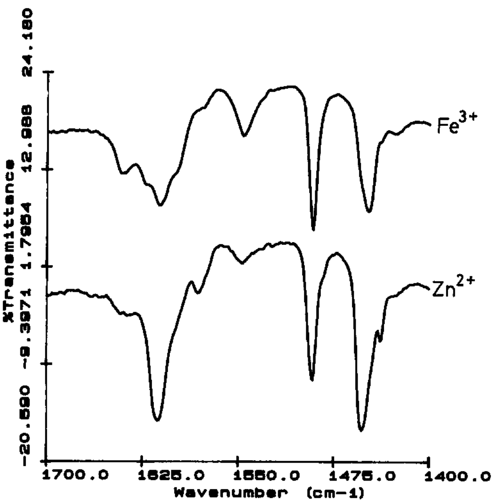

FIG. 2. IR spectra of pyridine adsorbed on Fe^{3+} and Zn^{2+}-exchanged montmorillonites. Brønsted acidity (band at 1545 cm^{-1}). Lewis acidity (band at 1450 cm^{-1}).

trolled by the nature of the cations (*1*); thus Zn^{2+} and Fe^{3+} were selected as exchange cations. Figure 2 reports the infrared spectra obtained on Fe^{3+}- and Zn^{2+}-exchanged montmorillonites evacuated at 120°C, after pyridine adsorption at room temperature, followed by desorption at the same temperature. Fe^{3+}-exchanged K10 montmorillonite exhibits stronger Brønsted acidity (band at 1545 cm^{-1}) and weaker Lewis acidity (band at 1450 cm^{-1}) than the corresponding Zn^{2+}-exchanged K10 montmorillonite (*16, 17*).

K10 montmorillonite is available from different sources; furthermore, the analysis of water and metallic ion contents show small but statistically significant differences between clays commercialized by Fluka and Süd Chemie (Table 1), so catalysts from both these sources were investigated.

The diene : dienophile ratio is a well-known factor influencing the results of the Diels–Alder reactions. Two levels were fixed with an excess of diene (3 : 1) and equimolar quantities of diene and dienophile (1 : 1).

Temperature is also a well-known factor influencing the reaction course. Normally, an increase in temperature leads to faster reaction rates, but lower endo/exo selectivities. We chose 20°C (i.e., a temperature close to room temperature) and −25°C as temperature levels.

The results obtained in clay-catalyzed organic reactions depend on the solvent used as the reaction medium. It has been suggested that this dependence is related to the coordinating ability of the solvent (*18*), so we chose two solvents with different donor ability, namely, dichloromethane and acetonitrile.

Finally, the ratio between catalyst and reagents is an important factor from a practical viewpoint. The upper level chosen (1 g of catalyst/3 mmol of dienophile) is that described by Laszlo and Moison (*8*d), whereas the lower level represents half the amount of catalyst with respect to the upper level (1 : 6).

For six factors and two levels, 64 experiments (2^6) are necessary to determine the coefficients of the main effects and all the possible interactions between two or more factors. However, if we assume that third and higher order interactions are negligible, it is possible to find subsets of the complete factoral design which still enable the coefficients of main effects and second-order interactions to be found. These subsets are called fractional replicates or fractional factorial designs (*14*).

In this case, a fractional factorial design of 16 experiments (2^{6-2}) was used initially. The coefficients of main effects (contaminated with third and higher order interactions) and those of paired (or aliased) second-order interactions can then be calculated. The latter means that individual coefficients for second-order interactions cannot be determined, but one can determine sums of two or three of them.

Table 3 gives the fractional factorial design used (experiments 1–16) and the results of the experimental measurements of the corresponding Diels-Alder reactions. As can be seen from the results described in Table 3, responses R_4 and R_5 are virtually identical. This means that adsorption of

TABLE 3

Experiments of the Fractional Factional Design and the Augmented Fractional Factorial Design with the Corresponding Experimental Responses

Experiment	F_1	F_2	F_3	F_4	F_5	F_6	R_1^a	R_2^b	R_3^c	R_4^d	R_5^e
1	−	−	−	−	−	−	0.1	1.5	2.3	5.7	6.0
2	+	−	−	−	+	−	15.3	10.1	28.3	15.9	16.0
3	−	+	−	−	+	+	30.8	6.7	63.1	20.2	19.6
4	+	+	−	−	−	+	1.6	1.6	7.0	14.9	15.6
5	−	−	+	−	+	+	43.6	50.7	85.0	19.0	20.3
6	+	−	+	−	−	+	3.0	9.0	16.8	13.2	12.6
7	−	+	+	−	−	−	0.4	3.0	5.3	5.3	5.8
8	+	+	+	−	+	−	18.5	39.3	60.5	22.1	21.9
9	−	−	−	+	−	+	3.6	25.8	30.2	4.6	4.8
10	+	−	−	+	+	+	9.7	2.4	9.5	6.0	5.8
11	−	+	−	+	+	−	45.6	48.1	46.2	11.2	11.3
12	+	+	−	+	−	−	3.2	15.4	16.1	5.8	5.7
13	−	−	+	+	+	−	61.0	71.1	74.8	10.6	10.7
14	+	−	+	+	−	−	16.2	65.2	69.0	6.4	6.4
15	−	+	+	+	−	+	10.2	68.8	71.1	4.5	4.5
16	+	+	+	+	+	+	65.1	69.0	72.9	13.2	13.1
17	−	−	−	+	+	+	45.8	43.8	45.3	9.4	9.7
18	+	+	−	−	+	+	17.7	10.2	17.7	14.5	12.8
19	−	+	+	−	+	−	11.4	53.2	58.4	20.5	20.3
20	+	+	−	+	+	−	15.2	15.4	14.7	10.1	10.3
21	+	+	+	+	−	+	10.8	62.8	65.0	4.7	4.7

[a] % Conversion at 2 h.
[b] % Conversion at 24 h.
[c] Overall yield at 24 h.
[d] Endo/exo ratio at 24 hr.
[e] Overall endo/exo ratio at 24 h.

products on the clay is not selective for endo or exo and therefore only R_4 will be considered throughout the work.

Analysis of the Factorial Design Results

The values of the coefficients calculated for the main effects and the aliased second-order interactions are given in Table 4. In order to obtain information about the statistical significance of these coefficients, replicates of experiments 10 and 16 (randomly chosen) were carried out, and with the corresponding calculated standard errors (2.61 for yields and 0.55 for endo/exo selectivities), a *t*-test was used to determine which coefficients were significant at a 95% level of probability. These are italicized in Table 4.

In the case of R_1 (percentage of conversion at 2 h), only F_5 (solvent) proves to be significant, although F_3 (diene : dienophile ratio) and F_4 (temperature) have high coefficients below the critical value. These results mean that, although higher concentration and temperature accelerate the initial reaction rate, the role of the solvent predominates in this aspect of the reaction. Thus, on average the reaction reaches a higher degree of conversion at 2 h in dichloromethane than in acetonitrile.

A rather surprising result is the nonsignificance of F_6 (catalyst : dienophile ratio), since a decrease in the relative concentration of catalyst is expected to reduce the initial reaction rate. One possible explanation of this result would be that the catalyst

TABLE 4

Coefficients of Main Effects and Interactions for Responses R_1 to R_4 Calculated with the Fractional Factorial Design (16 Experiments)

Factors	Coefficients[a]			
	R_1	R_2	R_3	R_4
F_1	−3.93	−3.99	−6.11	1.01
F_2	1.43	1.00	1.66	0.99
F_3	6.77	*16.53*	*15.79*	0.63
F_4	6.33	*15.25*	7.59	*−3.38*
F_5	*15.71*	6.69	*13.92*	*3.62*
F_6	0.46	−1.22	3.31	0.79
$F_1F_2 + F_3F_5$	4.10	3.81	2.48	0.84
$F_1F_3 + F_2F_5$	2.36	2.59	3.99	0.92
$F_1F_4 + F_5F_6$	0.64	−3.7	−0.73	−0.96
$F_1F_5 + F_2F_3 + F_4F_6$	−5.12	−2.99	−6.11	−1.48
$F_1F_6 + F_4F_5$	2.82	−4.76	*−11.78*	−1.15
$F_2F_4 + F_3F_6$	2.76	3.59	1.21	−1.00
$F_2F_6 + F_3F_4$	4.53	6.27	7.42	0.26
F_0 (mean effect)	20.50	30.49	41.14	11.16

[a] Italicized figures are significant to 95%.

is in excess even in the lower level. Additional experiments were carried out by decreasing the catalyst : dienophile ratio. The results are shown in Fig. 3, in which the initial conversion shows a linear dependence on the amount of catalyst at low catalyst : dienophile ratios, then reaches a plateau in the range of ratios used in the factorial design. At high catalyst amounts, the rate is limited by diffusion, and this explains the nondependence of R_1 with F_6.

The main factors affecting R_3 (overall yield after washing the clay) are F_3 (diene : dienophile ratio) and F_5 (solvent), although F_4 (temperature) also has a high coefficient. Thus the best yields are obtained in CH_2Cl_2 at 20°C and with the higher diene : dienophile ratio. In the case of R_2 (percentage of conversion after 24 h), F_3, F_4, and F_5 are again the most important factors, but the relative importance of F_4 and F_5 is reversed. The comparison of these results indicates that adsorption of products is more important at low temperatures and in CH_2Cl_2. In fact, Table 5, which gathers the averaged differences between R_3 and R_2 (i.e., the increase in the yield after washing the clay), shows that the adsorption effect is only important with CH_2Cl_2 at −25°C.

Finally, in the case of the endo/exo selectivity, R_4, the only significant factors are F_4 and F_5, with opposite signs, i.e., a decrease in temperature increases the endo/exo selectivity, as expected, as does the use of dichloromethane as solvent.

Going now to the second-order interactions, it would be interesting to have some additional information about those involving F_5 because of the importance of this factor in almost all responses.

Following the factorial design theory, a minimum of eight additional experiments are necessary in order to obtain individual coefficients for all second-order interactions. However, we are only interested in interactions involving F_5, therefore five additional experiments are enough to split all the desired paired interactions. These additional experiments were chosen using an exchange algorithm which searches for the *D*-optimality of the final experimental matrix, i.e., it tries to minimize the global variance of the calculated coefficients. This algorithm is implemented in the NEMROD package (*15*).

Table 3 gives the five additional experiments (17–21), and the corresponding experimental responses.

Most second-order interactions are not significant, excepting that for factors F_1F_5 in the case of R_2 (−10.10). One possible explanation of this interaction would lie in a larger adsorption of products in the case of Zn^{2+}-doped montmorillonite with respect to Fe^{3+}-doped montmorillonite. In fact, the effect of the adsorption (which exists only in the case of dichloromethane) is larger when the catalyst is a Zn^{2+}-doped montmorillonite.

To summarize the results described up to now, it can be said that three main factors influence the reaction course. First, the diene : dienophile ratio is an important factor influencing the final yield of the reaction, but it has no effect on the endo/exo selectivity and is only moderately important for the

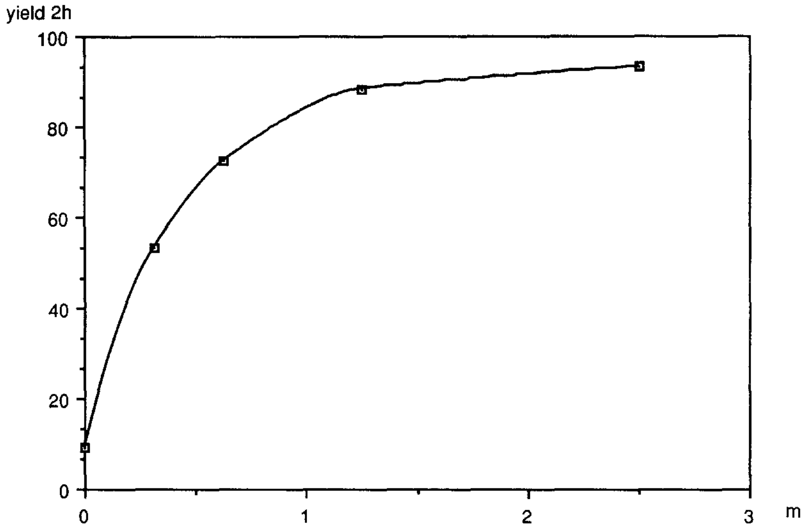

FIG. 3. Dependence of the initial reaction rate (yield after 2 h) on the amount of Zn^{2+}-clay in the reaction carried out at 20°C with 3 eq. of diene.

initial rate. Secondly, the temperature has only a moderate influence on the final yield and the initial rate, but is determinant on the endo/exo selectivity obtained. Finally, the solvent is important for the final yield, the initial rate and the endo/exo selectivity, so it seems to be the most determinant factor overall. Furthermore, it has been shown that there is a product-adsorption effect which depends on the solvent.

In connection with this, it is important to note that the role of the solvent on the endo/exo selectivity is very different in the case of non-catalyzed reaction. Thus, when the reaction is carried out in the absence of montmorillonite at 20°C, the endo/exo selectivities obtained are reversed with respect to the catalyzed process (3.7 for dichloromethane and 4.3 for acetonitrile versus 10.2 and 5.3, respectively, for the averaged values of the catalyzed reactions in the same conditions).

TABLE 5

Dependence of the Adsorption of Products ($R_3 - R_2$) on Temperature and Solvent

Temperature (°C)	Solvent	$R_2^{a,b}$	$R_3^{b,c}$	$R_3 - R_2^b$
20	CH_2Cl_2	47.6	50.8	3.2
20	CH_3CN	43.8	46.6	2.8
−25	CH_2Cl_2	26.7	59.2	32.5
−25	CH_3CN	3.7	7.8	4.1

[a] Conversion at 24 h.
[b] Averaged values from Table 3.
[c] Overall yield at 24 h.

Influence of the Solvent

In order to explain why the solvent is so important, and its role, additional experiments were carried out by keeping the other reaction conditions constant and using a reduced set of solvents with different physicochemical features.

In the clay-catalyzed Claisen rearrangement of allyl phenyl ethers, it has been suggested that the coordinating ability of the solvent, related to its basicity, is an important factor for explaining its influence on the reaction results (*18*). In view of this, a set of eight solvents was selected in order to cover a broad range of electron-donating ability, as described by Gutmann's DN pa-

TABLE 6

Results of the Reaction between Methyl Acrylate and Cyclopentadiene[a]

Solvent	Conversion (%)		Overall yield at 24 h. (%)	endo/exo at 24 h.	DN[b]	β_2^H[c]	Sp[d]	log P[e]
	15 min.	30 min.						
			Zn^{2+}-doped K10 montmorillonite					
1,4-Dioxane	—	4.2	39.9	4.2	14.8	0.41	0.0794	−0.42
Acetone	—	1.9	55.5	3.6	17.0	0.50	0.1267	−0.24
Acetonitrile	—	2.9	66.2	4.4	14.1	0.44	0.2167	−0.34
Cyclohexanone	—	8.5	78.7	3.4	—	0.52	—	−0.26
Diethyl ether	—	23.7	98.5	9.0	19.2	0.45	—	0.86
Dichloromethane	—	58.2	99.4	9.5	0.0	0.05	0.0000[f]	1.25
Anisole	37.9	65.9	100.0	10.9	—	0.26	—	2.10
Toluene	—	75.4	98.9	11.2	~0.0	0.14	0.0000[f]	2.73
			Fe^{3+}-doped K10 montmorillonite					
Acetonitrile	—	3.9	64.7	5.2	14.1	0.44	0.2167	−0.34
Diethyl ether	—	6.5	29.6	6.8	19.2	0.45	—	0.86
Dichloromethane	—	31.9	84.1	13.0	0.0	0.05	0.0000[f]	1.25
Anisole	46.9	48.5	48.3[g]	13.1	—	0.26	—	2.10
			95.0[h]	8.4[h]				
			Noncatalyzed reaction					
Dichloromethane	—	2.2	54.1	3.7	0.0	0.05	0.0000[f]	1.25
Acetonitrile	—	2.7	62.8	4.3	14.1	0.44	0.2167	−0.34
Anisole	—	3.1	72.8	3.2	—	0.26	—	2.10

[a] All the reactions were carried out at 30°C with a ratio diene : dienophyle = 3 : 1.
[b] Donor number. See Ref. (19).
[c] Hydrogen-bond basicity. See Ref. (*20*).
[d] Solvophobic power. See Ref. (*21*).
[e] Source: Ref (*22*).
[f] M. H. Abraham, personal communication.
[g] At this time an additional amount of cyclopentadiene (3 eq.) is added.
[h] Results obtained 24 h after the new addition of diene.

rameter (*19*) or Abraham's β_2^H hydrogen-bond basicity parameter (*20*). However, there are other solvent features which are known to influence the course of the Diels–Alder reaction (*4*), for example, polarity and solvophobicity (*21*), and they were also considered. Table 6 gives the list of solvents used in this series of experiments, together with some of their physicochemical features and the results of the reactions.

As can be seen, neither the reaction yield nor the endo/exo selectivity proved to be related to the solvent coordinating ability. Nevertheless, there is a qualitative relationship between rate (represented by the percentage of conversion after 30 min), overall yield after 24 h and endo/exo selectivity on the one hand and the hydrophobicity of the organic solvent (represented by log *P*, the octanol/water partition coefficient (*22*)) on the other. Thus, hydrophobic solvents show good results, whereas, in hydrophilic solvents, a comparison of the results with those obtained in noncatalyzed processes (*4*d) seems to show that most of the reaction takes place in the bulk of the solvent, so the clay does not play a catalytic role.

In view of these results two questions arise: why is acetonitrile unsuitable as a solvent for this reaction and why does anisole show such different behaviour as a function of the cation? In order to find an answer to these questions several experiments were carried out.

The adsorption isotherms of methyl acrylate in Zn^{2+}-doped K10 montmorillonites were performed from methylene chloride and acetonitrile at 20 and −25°C. The results obtained from these experiments are shown in Fig. 4, where the initial concentration of this reagent in the Diels-Alder reaction is indicated. As can be seen, the adsorption from acetonitrile is lower than from

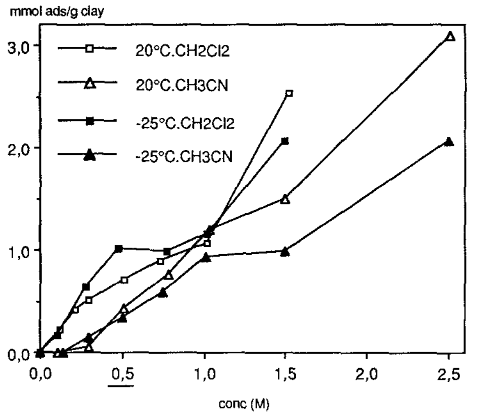

FIG. 4. Adsorption isotherms of methyl acrylate on Zn^{2+}-exchanged montmorillonite from solutions in acetonitrile and in methylene chloride. The initial concentration used in Diels–Alder reactions is underlined.

methylene chloride, but not so low as to account for the noncatalytic effect of the clay in this solvent. In fact, although the adsorptions from 1 *M* solution of methyl acrylate in both solvents are similar, the Diels–Alder reactions carried out at 20°C, with this concentration of dienophile, show the abovementioned influence of the solvent (CH_2Cl_2: 63.9% in 30 min with endo/exo = 9.8; CH_3CN: 5.6% in 30 min with endo/exo = 4.4).

This behaviour may be due to a lack of adsorption of cyclopentadiene from acetonitrile solutions. Unfortunately, the tendency of cyclopentadiene to dimerize prevents the realization of reliable adsorption studies. In fact, when solutions of 1.485 g of cyclopentadiene, in 15 ml of methylene chloride and acetonitrile, were kept at 20°C for 24 h in the presence of 1.25 g of Zn^{2+}-doped K10 montmorillonite, 0.7 g of a yellowish oil were obtained in both solvents.

Further insight into the differences between methylene chloride and acetonitrile was achieved by an IR study of the adsorption of methyl acrylate on wafers of Fe^{3+} and Zn^{2+}-doped clays. The wafers were left to stand for 24 h in solutions of methyl acrylate in methylene chloride and acetonitrile, reproducing the concentration used in the Diels–Alder reactions. They were then washed with CCl_4 and the IR spectrum was registered. Figure 5 shows the IR spectra of the wafers of Zn^{2+}-doped clay resulting from this treatment. As can be seen, in the spectrum of the clay treated in acetonitrile only the bands corresponding to molecular water, structural vibration of the clay and CN vibrations appear. Nevertheless, the clay treated in CH_2Cl_2 shows a carbonyl band (1695 cm^{-1}) which is shifted from its position in solution (1725 cm^{-1} in methylene chloride), so the dienophile is coordinated to an acid center of the clay. The Fe^{3+}-doped clay exhibits the same behavior.

Adsorption isotherms indicate the adsorption of dienophile in the clay from solutions in acetonitrile. However, the lack of a carbonyl band in the IR study shows that the dienophile is eliminated from the clay by washing with CCl_4. Therefore, the abovementioned adsorption is very weak and probably takes place on the surface of the clay.

By contrast, adsorption of dienophile from solutions in methylene chloride is stronger and coordination of methyl acrylate to acidic sites in the clay takes place. This coordination probably occurs deep within the interlayer region, where the majority of the exchangeable cations are to be found. The change of volume during the reaction is small enough to allow the reaction to take place in this region (a sphere with the volume of the transition state (*23*) has a diameter of 7.6 Å).

Adsorption isotherms of the major product, endo cycloadduct, show that adsorption of products increases when the temperature decreases, which is specially significant when the adsorption from solutions in acetonitrile is considered. At −25°C adsorptions of cycloadduct from methylene chloride and from acetonitrile are similar (Fig. 6). Hence the lack of adsorption of products in the reactions carried out in acetonitrile at −25°C must be due to the low chemical yield obtained.

Table 6 shows that the Fe^{3+}-doped clay-

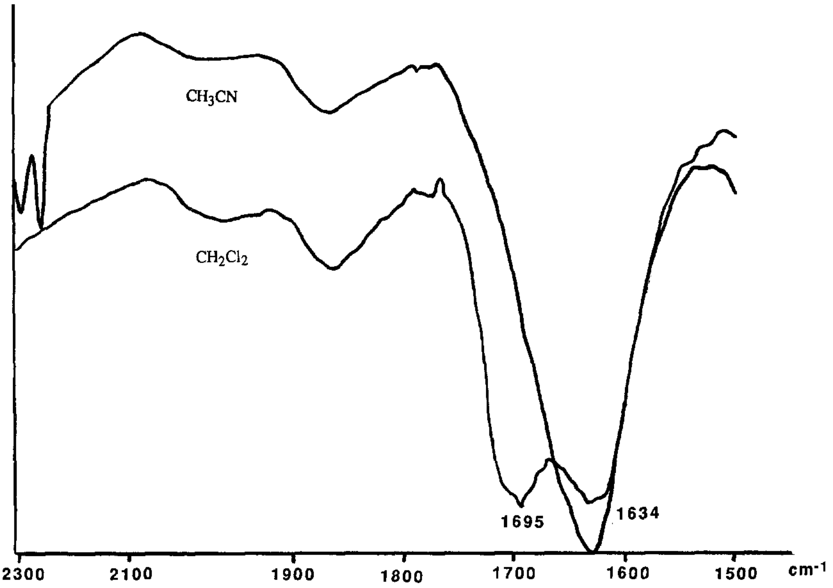

FIG. 5. IR spectra of Zn^{2+}-exchanged montmorillonite after adsorption from solutions of methyl acrylate in acetonitrile and in methylene chloride.

catalyzed reaction carried out in anisole is very fast, but after 30 min there is no further conversion. However, when an additional amount of diene is added the reaction continues but with a decrease of the endo/exo selectivity, which indicates that the reaction is partially noncatalyzed.

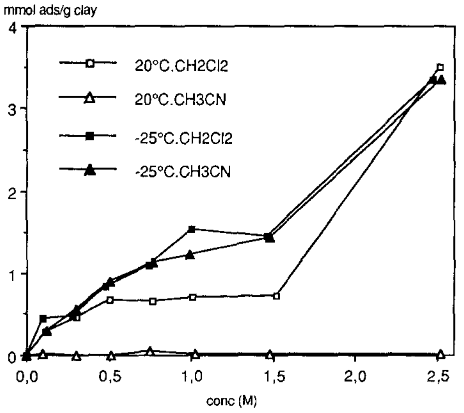

FIG. 6. Adsorption isotherms of endo cycloadduct on Zn^{2+}-exchanged montmorillonite from solutions in acetonitrile and in methylene chloride.

Several authors have shown (*8*a, *24*) that dimerization of dienes catalyzed by clays is a radical-promoted reaction. In particular, Laszlo and Luchetti (*8*a) have reported that dimerization of cyclohexadiene is promoted by doped K10 montmorillonites in the presence of 4-tert-butyl phenol, which is known to generate radical cations (*25*). Catalytic activity for this dimerization depends on the type of cation exchanged in the clay, and the best results have been obtained with Fe^{3+}.

In view of these reports it was speculated that the low activity for methyl acrylate cyclopentadiene cycloaddition on Fe^{3+}-doped clay in the presence of anisole could be attributed to a radical-promoted disappearance of cyclopentadiene by parallel reactions. Some of the products resulting from these reactions were identified as adducts 1 : 1 and 1 : 2 of anisole and cyclopentadiene, by gas-chromatography–mass-spectrometry. Cyclopentadiene is also eliminated from the reaction medium via oligomerization; a polymer fraction was detected by precipitation with methanol from the reaction me-

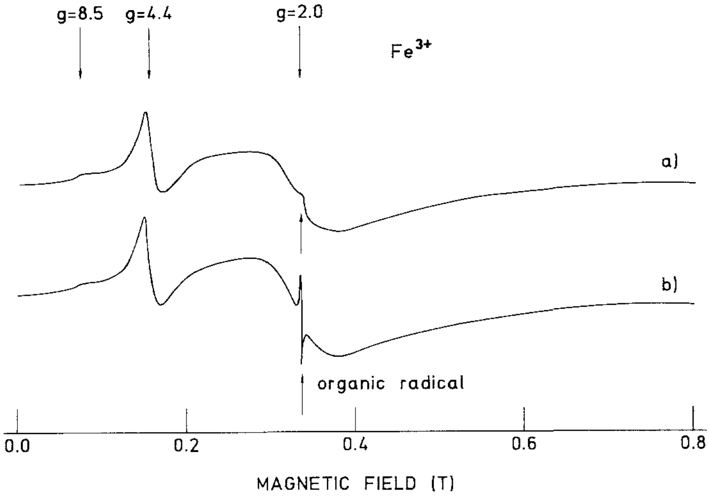

FIG. 7. ESR spectra of (a) Fe^{3+}-exchanged montmorillonite and (b) after saturation with anisole.

dium. The byproducts resulting from these parallel reactions deactivate the clay, which accounts for the decrease in endo/exo selectivity observed when an additional amount of diene is added (Table 6).

These parallel reactions are minimized in the presence of the Zn^{2+}-doped K10 montmorillonite, because of the lower tendency of this cation to promote the formation of radicals in the presence of phenolic compounds (*8*a). This hypothesis was checked by ESR analysis of the initial samples and of the same samples saturated with different solvents.

The spectra of both Fe^{3+} and Zn^{2+} clays dried at 120°C (Fig. 7) show a complex signal with a narrow asymmetric line at $g \sim 4.4$, with a shoulder on the low field side ($g \sim 8.5$) and a very broad line centered at $g \sim 2$. This spectrum is typical of Fe^{3+} in a high crystal field (*26*), and is not changed by the addition of either methylene chloride, diethyl ether, anisole, or methyl acrylate.

There is also a much narrower signal ($\Delta H_{pp} \sim 1$ mT) at $g = 2.004 \pm 0.002$, which could be characteristic of free radicals. The presence of this very weak signal in the initial solid could be attributed to traces of organic material adsorbed on the clay. Upon anisole addition, the intensity of this signal increases by a factor of 10 in the case of the Fe^{3+} clay but remains unchanged in the case of the Zn^{2+} sample. The original narrow signal of the clay at $g = 2.004$ is not modified by the addition of methylene chloride, diethyl ether or methyl acrylate, and it can be concluded that the new signal appearing upon anisole addition is characteristic of radical formation induced by the interaction of anisole with the Fe^{3+} clay.

It can be concluded that, in the absence of radicals (Zn^{2+}-doped K10 montmorillonite), the Diels–Alder reaction of carbonyl-containing dienophiles is faster than diene dimerization or other lateral reactions. In the presence of radicals the Diels–Alder reaction is promoted (the conversion of methyl acrylate after 15 min on Fe^{3+}-doped K10 montmorillonite is higher than on Zn^{2+}-doped K10 montmorillonite in anisole as solvent, see Table 6), but lateral reactions are also faster and overall reaction yield is lower.

Influence of the Exchanged Cation

The coefficients obtained in the analysis of the factorial design indicate that F_1 (exchanged cation) is not a significant factor.

TABLE 7

Coefficients of Main Effects and Interactions for Responses R_1 R_3, and R_4 Calculated with the 2^3 Factorial Design (CH_2Cl_2)

Factors	Coefficients[a]		
	R_1	R_3	R_4
F_1	*−9.1*	*−12.2*	−0.5
F_3	*10.9*	*18.3*	1.5
F_4	*9.1*	−4.2	*−4.5*
F_1F_3	3.8	5.6	1.9
F_1F_4	1.1	2.6	−0.2
F_3F_4	6.9	4.7	0.2
$F_1F_3F_4$	6.2	3.1	0.1
F_0 (mean effect)	36.2	55.6	14.8

[a] Italicized figures are significant to 95%.

However, one half of the experiments have been carried out in acetonitrile, where the clay has been shown not to play any catalytic role, so a further analysis is needed. If only the experiments carried out in methylene chloride are considered, the coefficients calculated for first order effects are contaminated with second-order interactions. However, taking into account that F_2 and F_6 are not significant a 2^3 factorial design for F_1 (exchanged cation), F_3 (diene : dienophile ratio), and F_4 (temperature) can be considered with only the experiments carried out in CH_2Cl_2 (Table 1, experiments 2, 3, 5, 8, 10, 11, 13, and 16). The analysis of this factorial design leads to the coefficients gathered in Table 7, where the significant coefficients are italicized. As can be seen, there is not any significant interaction. F_3 (diene : dienophile ratio) shows the above-described influence on the results obtained. However, F_4 (temperature) does not show a significant influence on the overall yield, which seems to indicate that its effect is only relevant in reactions carried out in acetonitrile. With regard to F_1 (exchanged cation) the Zn^{2+}–K10 montmorillonite favours high reaction rates and overall yields, but this factor does not have any influence on the endo/exo ratio.

It can be concluded that the clay with the greater Lewis acidity is the more efficient catalyst.

CONCLUSION

Experimental factorial design has proved to be a useful tool for studying several factors influencing clay-catalyzed Diels-Alder reactions. This study shows the expected influences for the temperature and the diene : dienophile ratio. The influence of the exchanged cation indicates that Zn^{2+}–K10 montmorillonite, with a greater Lewis acidity than the Fe^{3+}-clay, is a more efficient catalyst. This study shows that the most important parameter is the nature of the solvent. Hydrophilic solvents appear to be inadequate for this type of reaction. Furthermore, an interaction exists between the solvent and the nature of cations exchanged into the clay. In particular, the association of anisole with easily reducible cations such as Fe^{3+} induces undesirable radical reactions. From a practical point of view, the use of organic solvents with the clay has two advantages over the use of water as solvent: much larger concentrations of reagents can be reached in organic solvents and temperatures below 0°C can be used, which greatly increases the endo/exo selectivity.

ACKNOWLEDGMENTS

This work was made possible by the generous financial support of the Comisión Interministerial de Ciencia y Tecnología (Project MAT90-0778). J. M. Fraile thanks the Ministerio de Educación y Ciencia for a grant. We are also indebted to the Subdirección General de Cooperación Internacional (Acción Integrada Hispano-Francesa 243 B).

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