Comparison of $AlEt_2Cl$ and $ZnCl_2$ supported on silica gel as catalysts of Diels–Alder reactions. Influence of the nature of the dienophile

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Non-modified silica gel, silica gel treated with $AlEt_2Cl$, and $ZnCl_2$ supported on silica gel are tested as catalysts in the Diels–Alder reactions of cyclopentadiene (1) with methyl acrylate (2a), (–)-menthyl acrylate (**2b**) and acrylonitrile (2c). In general, supported catalysts are more efficient than non-modified silica gel. Two different kinds of silica gel are tested and the amount of aluminium incorporated when they are treated with $AlEt_2Cl$ changes from one to another, which influences the chemical yield but not the selectivity of the reactions. In general, aluminium catalysts are more efficient than $ZnCl_2$-supported ones in the reactions of acrylates, but the latter solid is a better catalyst in the reactions of acrylonitrile (2c). Differences in acid strength and hardness of the catalytic sites are invoked to account for these results.

Keywords: Diels–Alder; heterogeneous catalysis; asymmetric synthesis; $ZnCl_2$/silica; $AlEt_2Cl$/silica

1. Introduction

$ZnCl_2$ supported on an acid-treated clay, K10 montmorillonite (known as clayzic), is a remarkably active catalyst in the Friedel–Crafts alkylation of benzene with benzyl chloride [1]. It has been shown that this support is similar to silica, and $ZnCl_2$ supported on porous silica, $ZnCl_2/SiO_2$, is a catalyst similar to clayzic [2]. The results obtained with these solids indicate that they behave as acid catalysts and, particularly, as Lewis acid catalysts. Despite the high activities of these catalysts in simple alkylation reactions, they have shown rather disappointingly low activities in reactions involving polar reagents, for example in the alkylation of anisole rather than benzene [3], and in Friedel–Crafts acylations in general [4].

In view of these results we wondered whether the catalytic activity of these solids was limited to a few Friedel–Crafts alkylations or whether they could be used in a wider range of reactions, some of which involve more polar reagents. The Diels–Alder reaction of acrylic acid derivatives is an example of Lewis acid-catalyzed organic reaction where one of the reagents, the dienophile, is quite polar.

It has been shown that silica gel [5–7] or silica gel modified by treatment with aluminium or titanium derivatives [6,7] catalyze some Diels–Alder reactions. In particular, silica gel treated with $AlEt_2Cl$ is an excellent catalyst for the reactions of non-chiral and chiral acrylates [6]. This solid was selected to compare its catalytic activity with that of $ZnCl_2$ supported on silica gel, and with that of the silica gel used alone, in the Diels–Alder reactions of cyclopentadiene (**1**) with three different dienophiles: methyl acrylate (**2**a), (–)-menthyl acrylate (**2b**) and acrylonitrile (**2**c) (scheme 1).

2. Experimental

EP11–Al and SiO_2–Al were prepared from silica gel EP11 from Crossfield, and Merck silica gel 60, respectively, using the previously described method [6]. EP11–Zn was obtained from silica gel EP11 and $ZnCl_2$ as previously described [2].

Reactions of methyl acrylate (2a) and (–)-menthyl acrylate (**2b**) with cyclopentadiene (1) were monitored by gas chromatography using the analytical methods previously described [8].

Reactions of acrylonitrile (2c) with cyclopentadiene (1) were monitored by gas chromatography (GC) using 1,2-dichloroethane as internal standard (FID from Hewlett–Packard 5890 II, cross-linked methyl silicone column 25 m × 0.2 mm × 0.33 μm, helium as carrier gas 17 psi, injector temperature: 230°C, detector temperature: 250°C, oven temperature program: 50°C (3 min)–25°C/min–90°C (10 min), retention times: 2.81 min (1,2-dichloroethane), 12.37 min (endo cycloadduct, **3nc** + **4nc**), 11.24 min (exo cycloadducts, **3xc** + **4xc**)).

Reactions in toluene. Under argon, 7.48 mmol of the corresponding dienophile (**2**) and 494 mg (7.48 mmol) of

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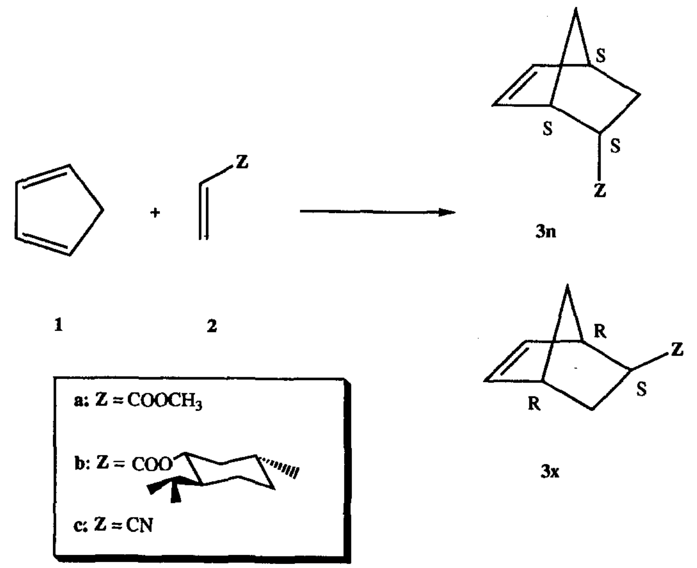


Scheme 1.

Table 1
Results obtained in the reactions of cyclopentadiene (1) with methyl acrylate (2a), (–)-menthyl acrylate (**2b**), and acrylonitrile (2c) in toluene without a catalyst or in the presence of unmodified silica gel, at room temperature [a]

Catalyst	Dienophile	Time (h)	% conversion [a]	Endo/exo [a]	% de [a,b]
none	2a	0.5	0.5	2.7	–
		3	3.5	2.7	–
		24	25.5	2.7	–
	2b	1	0.5	1.8	8
		3	1.5	1.8	8
		24	10.0	2.8	10
	2c	0.5	3.5	1.2	–
		3	6.0	1.2	–
		24	24.0	1.2	–
SiO_2 [c]	2a	0.5	7.0	5.8	–
		1	11.0	5.9	–
		3	35.5	5.9	–
		24	95.5	5.9	–
	2b	1	3.5	2.2	13
		3	14.0	4.2	13
		24	38.0	4.2	13
	2c	0.5	3.5	1.2	–
		1	4.0	1.2	–
		3	11.0	1.2	–
		24	61.0	1.3	–
EP11 [d]	2a	0.5	0.5	3.7	–
		1	1.0	4.2	–
		3	4.5	3.5	–
		24	28.5	3.7	–
	2b	1	1.0	4.3	18
		3	4.0	3.8	18
		24	17.5	3.7	13
	2c	0.5	4.0	1.4	–
		3	5.0	1.2	–
		24	21.0	1.2	–

[a] Determined by GC.
[b] **4n** is the major product.
[c] SiO_2: Merck silica gel 60 (476 $m^2\,g^{-1}$).
[d] EP11: silica gel EP11 from Crossfield (415 $m^2\,g^{-1}$).

freshly distilled cyclopentadiene (**1**) were added with a syringe to a suspension of the corresponding catalysts (1 g) in dry toluene (15 ml). The mixture was stirred at room temperature and the reaction was monitored by GC. After the corresponding time (tables 1–3) the catalyst was removed by filtration, repeatedly washed with methylene chloride and the solution was analyzed by GC. Reference reactions were carried out under exactly the same conditions without a catalyst.

Reactions in the absence of a solvent. A solution of 1 mmol of the corresponding dienophile in dry methylene chloride was mixed with 1 g of the corresponding catalyst, and the solvent was removed under reduced pressure. 198 mg (3 mmol) of freshly distilled cyclopentadiene was added with a syringe. The mixture was shaken for the corresponding time (tables 1–3) and after this time methylene chloride was added. The catalyst was removed by filtration, repeatedly washed with methylene chloride, and the solution was analyzed by GC. Reference reactions were carried out under exactly the same conditions without a catalyst.

3. Results and discussion

Table 1 shows the effect of the unmodified silica gel (Merck Silica Gel 60 and EP11 from Crossfield) on the reactions carried out in toluene. In all cases, the addition of silica gel slightly improves the conversion at low reaction times, as well as the overall conversion and the selectivity. However, the observed effects are not very important and similar results can be reached carrying out the reactions in solvents more polar than toluene, such as methanol or acetonitrile. Even better results are obtained in solvents with high hydrogen bond donor (HBD) ability, such as 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) [9,10]. These effects are more noticeable with the silica gel from Merck, which has a higher surface

Table 2
Results obtained in the reaction of cyclopentadiene (**1**) with methyl acrylate (**2a**), (–)-menthyl acrylate (**2b**), and acrylonitrile (**2c**) in toluene in the presence of Lewis acid modified silica gel, at room temperature

Catalyst	Dienophile	Time (h)	% conversion [b]	Endo/exo [b]	% de [b,c]
SiO_2–Al [a]	**2a**	0.5	90.5	19.8	–
		1	92.0	19.8	–
		2	98.0	19.7	–
	2b	0.5	70.0	12.2	35.6
		1	79.0	12.1	35.6
		2	89.0	11.9	35.6
		7	95.0	11.6	35.6
	2c	0.5	12.5	1.6	–
		1	16.0	1.8	–
		3	29.0	1.9	–
		24	42.5	1.9	–
EP11–Al [b]	**2a**	0.5	70.0	21.0	–
		3	70.0	20.2	–
		24	73.5	19.6	–
	2b	1	41.0	10.6	33.5
		2	41.0	10.6	33.0
		3 [c]	92.5	11.2	36.3
	2c	0.5	4.5	1.2	–
		1	7.0	1.3	–
		24	39.5	1.3	–
EP11–Zn [d]	**2a**	0.5	41.0	12.0	–
		1	55.0	11.9	–
		3	67.0	11.9	–
		24	74.5	11.9	–
	2b	0.5	17.5	8.2	38.9
		1	28.0	8.2	38.9
		3	35.5	8.2	38.9
		24	41.3	8.2	38.9
	2c	0.5	21.0	1.8	–
		1	33.0	2.0	–
		3	50.0	1.9	–
		24	79.0	2.0	–

[a] SiO_2 treated with $AlClEt_2$ (1.44 mmol Al per gram of catalyst, determined by Plasma Emission Spectroscopy).
[b] EP11 treated with $AlClEt_2$ (0.60 mmol Al per gram of catalyst, determined by Plasma Emission Spectroscopy).
[c] After 2 h an additional equivalent of diene is added.
[d] $ZnCl_2$ supported on EP11 (2.2 mmol Zn per gram of catalyst).

Table 3
Results obtained in the reaction of cyclopentadiene (1) with methyl acrylate (2a), (–)-menthyl acrylate (**2b**), and acrylonitrile (2c) without a catalyst or in the presence of unmodified silica gel, in the absence of a solvent at room temperature

Catalyst	Dienophile	Time (h)	% conversion	Endo/exo	% de
none	2a	1	52.5	3.1	–
		24	95.5	2.7	–
	2b	1	19.0	2.9	9.1
		24	72.0	2.0	4.1
	2c	1	24.5	1.5	–
		24	46.5	1.2	–
SiO_2	2a	1	52.5	8.7	–
		24	100.0	8.5	–
	2b	1	32.5	9.0	16.3
		24	99.5	9.0	17.7
	2c	24	44.5	1.6	–
EP11	2a	1	28.0	10.0	–
		24	90.0	8.6	–
	2b	1	40.0	10.1	21.9
		24	96.0	9.0	20.6
	2c	24	40.5	1.8	–

area. As a consequence, it can be concluded that silica gel displays a solvent-like or bulk effect. In fact, it can be thought that the coordination of the dienophile to the silanol groups increases its reactivity, this effect being analogous to that produced with HBD solvents.

It is worth noting that, in the absence of silica gel, acrylonitrile (2c) reacts faster than acrylates 2a and **2b**, and higher percentages of conversion are observed at short reaction times. However, the relative reactivity is reversed by addition of the solid. This behaviour is also observed in the non-catalyzed homogeneous reactions, in which the influence of the different solvent properties on the reaction results strongly depends on the nature of the reagents [9].

Table 2 gathers the results obtained in the reactions carried out in toluene in presence of supported Lewis acids. First of all, a practical conclusion must be emphasized, namely that *it is possible to obtain very high percentages of conversion with good selectivities without using an excess of diene.*

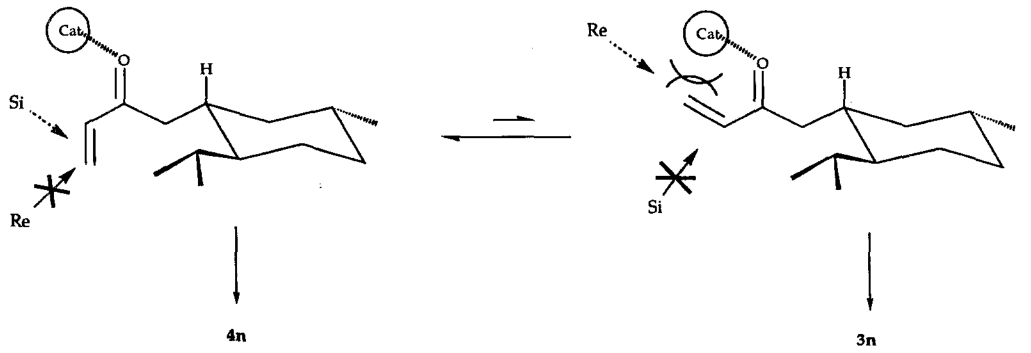
All the three reactions are promoted by the three solids, although the catalytic effect depends on the dienophile and on the nature and amount of catalytic sites. With both acrylates (**2b** and 2c) the order of catalytic activity is: SiO_2–Al > EP11–Al > EP11–Zn. Supported aluminium catalysts are more active than supported $ZnCl_2$, in line with the accepted Lewis acid strengths of tetrahedral Al(III) and Zn(II) centres. The difference between SiO_2–Al and EP11–Al may be due to the different Al functionalization on the two supports.

The endo/exo selectivities obtained with both acrylates depend on the nature and not on the amount of the catalytic sites. Thus, both Al catalysts display similar selectivities, which are significantly better than that obtained with the supported $ZnCl_2$.

In the reaction of cyclopentadiene with (–)-menthyl acrylate (**2b**), a second selectivity, namely the diastereofacial selectivity (asymmetric induction) exists. The diastereomeric excess is significantly increased by the presence of all the three catalysts. Unlike the observed for the endo/exo selectivity, the asymmetric induction does not depend on the nature of the catalytic sites. It has been shown that the asymmetric induction obtained in Diels–Alder reactions of chiral acrylates strongly depends on the s-cis/s-trans conformational equilibrium of the chiral dienophile [10,11], given that both conformers display reversal topicity in their top and bottom faces. Thus, the attack of the cyclopentadiene on the less hindered bottom face (Si face) of the s-trans conformer leads to **4n** as the major product. On the other hand, the attack of the diene on the bottom face (Re face) of the s-cis conformer leads preferentially to **3n**. The coordination of the catalyst shifts the conformational equilibrium towards the s-trans conformer due to steric reasons (scheme 2). The results obtained with Lewis acid-supported silicas clearly indicate that this coordination takes place in all cases. Therefore, the differences observed in rate and endo/exo selectivity between aluminium and zinc catalysts must be due to the different electronic nature of the dienophile/active site complexes.

The results obtained for the reaction of cyclopentadiene (**1**) with acrylonitrile (2c) show that EP11–Zn is the most active catalyst, exhibiting both the highest activity and the greatest selectivity. It is worth noting that this solid is the best heterogeneous catalyst described so far for Diels–Alder reactions of α,β-unsaturated nitriles, and that impressively high conversions are obtained without excess of either reagent.

The relatively high activity of supported Zn compared to supported Al catalysts in this reaction is not reflected in homogeneous systems. For instance, in the Diels–Alder reaction of 2-methyl-1,3-butadiene (iso-



Scheme 2.

prene) with acrylonitrile under homogeneous catalysis, $AlCl_3$ is by far more active than $ZnCl_2$ [12].

The $ZnCl_2$ loading on EP11–Zn is higher than the Al loading on both EP11–Al and SiO_2–Al, but this seems not sufficient to account for the difference in activities observed. Indeed, a comparison of the activities of the two Al-supported catalysts (which have different Al loadings) shows that, within limits, activity is not particularly sensitive to metal loading. A more acceptable explanation is that the catalyst with the softest catalytic sites is the most active in the reactions of the softest dienophile.

It is worth mentioning that the overall conversions obtained in this reaction with both Al-supported catalysts are low, which must be due to the known existence of relatively favourable competing reactions. In fact, not only diene polymerization, which is common place for the three reactions studied, but also polymerization of the dienophile, and copolymerization of both reagents, can account for this result. The results obained with EP11–Zn indicate that this solid may be a suitable catalyst for the Diels–Alder reactions of acid-sensitive reagents.

Tables 3 and 4 gather the results obtained in the reactions carried out in the absence of a solvent. The general conclusions are similar to those reached for the reactions carried out in toluene, namely that unmodified silicas cannot be considered as true catalysts, whereas supported Al and Zn solids promote the reactions and noticeably increase the selectivities. In comparison with the reactions carried out in toluene, slightly better endo/exo selectivities are obtained.

It is interesting to note that the use of this method is not advantageous in the reaction of cyclopentadiene (**1**) with acrylonitrile (**2c**). In spite of using an excess of diene the overall conversions are not noticeably improved and they are even worse than that obtained with EP11–Zn in toluene. This result points to an increase of undesirable polymerization reactions under these conditions.

To summarize, all the three solids obtained by supporting Lewis acids on silica gel are suitable catalysts for the reactions studied. Aluminium catalysts are better for the reactions of acrylates. In these cases, the reaction rate depends on the aluminium loading, but neither the endo/exo nor the diastereofacial selectivities depend on

Table 4
Results obtained in the reaction of cyclopentadiene (**1**) with methyl acrylate (**2a**), (−)-menthyl acrylate (**2b**), and acrylonitrile (**2c**) in the presence of a Lewis acid modified silica gel, in the absence of a solvent at room temperature

Catalyst	Dienophile	Time (h)	% conversion	Endo/exo	% de
SiO_2–Al	2a	1	100.0	23.2	–
	2b	1	99.0	15.6	28.8
	2c	1	35.0	1.8	–
		24	55.0	1.8	–
EP11–Al	2a	1	100.0	19.0	–
	2b	1	81.0	15.6	37.0
		24	98.0	15.6	37.4
	2c	1	38.0	1.8	–
		24	55.5	1.8	–
EP11–Zn	2a	1	100.0	14.7	–
	2b	1	87.5	9.1	38.1
		24	100.0	10.1	18.5
	2c	1	38.5	2.2	–
		24	41.5	2.2	–

this factor. The EP11–Zn is an excellent catalyst for the reaction of cyclopentadiene with acrylonitrile, which can be accounted for by the softest character of the catalytic sites and by a minor concurrence of lateral polymerization reactions. This result makes EP11–Zn a promising catalyst for the otherwise difficult Diels–Alder reactions of acid-sensitive reagents.

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