

Silica and Alumina Modified by Lewis Acids as Catalysts in Diels-Alder Reactions of Chiral Acrylates

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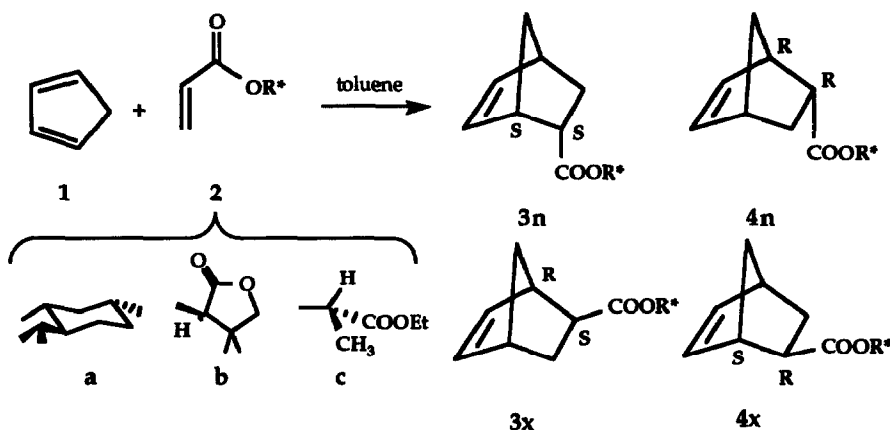
Abstract: Silica and alumina, modified by treatment with AlClEt_2 and TiCl_4 , are tested as catalysts in the reactions of cyclopentadiene (**1**) with (-)-menthyl acrylate (**2a**), (R)-O-acryloyl pantolactone (**2b**) and (S)-O-acryloyl lactate (**2c**). Silica-modified systems are the most efficient heterogeneous catalysts described to date for this kind of reaction, leading to selectivities similar to those obtained with aluminium homogeneous catalysts. Whereas silica- AlClEt_2 is better for the reaction of **2a** and **2c**, silica- TiCl_4 is more suitable for the reaction of **2b**.

The Diels-Alder adducts of acrylic acid derivatives constitute an important class of compounds as key intermediates for the total synthesis of a variety of natural products.¹ They are usually obtained by Lewis acid-catalysed reactions. However, the use of these catalysts has its drawbacks, such as the disposal of environmentally hazardous residues. Therefore, a great deal of effort has been devoted to the development of heterogeneous systems able to catalyse these reactions, and several inorganic solids (silica gel,^{2,3} magnesium silicate,³ alumina,^{3,4} zeolites,⁵ and clays⁶) have proved to be efficient catalysts.

Excellent diastereofacial selectivities have been achieved in asymmetric Diels-Alder reactions between prochiral 1,3-dienes and chiral acrylates using Lewis acids as homogeneous catalysts.⁷ Alumina has been tested as a catalyst in the reactions of cyclopentadiene with (-)-menthyl acrylate and di-(-)-menthyl fumarate,⁸ whereas clays have been used as catalysts in the reactions of cyclopentadiene with (-)-menthyl acrylate⁹ and (R)-O-acryloyl pantolactone.¹⁰ With the latter, asymmetric inductions of about 50% have been obtained, but their catalytic activity is far from that of homogeneous catalysts. Thus, it is of interest to search for solids with better catalytic activity.

In view of the high activity associated with tetrahedral aluminium Lewis acids, Drago and Getty¹¹ have prepared solids with strong Lewis acidity by the reaction of inorganic solids with aluminium chloride. We have used a similar strategy to support aluminium and titanium Lewis acids on silica and alumina. In this communication we describe our first results using silica and alumina, modified by treatment with AlClEt_2 and TiCl_4 , as catalysts in the reactions of cyclopentadiene (**1**) with some chiral acrylates, namely (-)-menthyl acrylate (**2a**), (R)-O-acryloyl pantolactone (**2b**) and (S)-O-acryloyl lactate (**2c**).

Alumina (Merck aluminium oxide 60, 63-200 nm) was activated by heating under vacuum at 140°C (Al1) or at 400°C (Al2). Silica gel (Merck silica gel 60, 63-200 nm) was activated by heating under vacuum at 140°C (Si1). The activated solids were then refluxed with solutions of AlClEt_2 and TiCl_4 in toluene. The excess of Lewis acid was eliminated and the solids obtained were used as catalysts in the reactions of cyclopentadiene (1) with (-)-menthyl acrylate (2a), (R)-O-acryloyl pantolactone (2b) and (S)-O-acryloyl lactate (2c) (Scheme 1).



Scheme 1

Table 1 gathers the results obtained. For the reactions of **2a**⁹ and **2b**¹⁰, absolute configurations of the major cycloadducts were assigned as previously described. In the case of **2c**, **3n** and **4n** the absolute configurations were assigned by means of the HPLC analyses of the previously described reactions in solution.¹²

Silica-modified catalysts were found to be more efficient than alumina-modified ones, the latter being particularly sensitive to decrease in temperature. With the former catalysts, high conversions and *endo/exo* selectivities are obtained in short times and without a large excess of diene, so that their catalytic activity is not very far from that of homogeneous catalysts; particularly if the amount of aluminium (1.4 meq/g) or titanium (1.2 meq/g) incorporated¹³ is taken into account.

When **2a** is used as a chiral dienophile, **4n** is preferably obtained, which is accounted for by the previously described model.^{7,10} The diastereomeric excess obtained (40%) is slightly smaller than that obtained with clays,⁹ but is clearly better than the excess obtained in the same reaction catalysed by non-modified alumina.⁸

Clear differences are observed when the results obtained from the reactions of **2b** and **2c** are compared. With the former dienophile, Si1· TiCl_4 leads to better conversions and selectivities than Si1· AlClEt_2 , whereas the converse is true when **2c** is used as a dienophile. These results suggest that a correlation between the nature of the supported metal and the dienophile exists. Furthermore, the low asymmetric inductions obtained with alumina catalysts show that the nature of the support also plays an important role.

The TiCl_4 -catalysed,¹⁴ AlClEt_2 -catalysed,¹⁰ and non-catalysed¹⁰ reactions of **2b** with cyclopentadiene have been previously studied. The asymmetric inductions obtained in these reactions,

Table 1. Results obtained from the Diels-Alder reactions of 1 with 2a, 2b and 2c in toluene.

Dienophile	catalyst (g/mmol of 2)	ml toluene/ mmol of 2	T (°C)	1:2	t (min)	conversion ^a (%)	endo/exo ^b	de ^c (%)
2a	AlI· AlClE ₂ (1.42)	2	20	6	150	63	88:12	40
	Al2· AlClE ₂ (1.42)	2	20	6	150	86	87:13	40
	AlI· TiCl ₄ (1.42)	2	20	6	420	63	89:11	40
	Al2· TiCl ₄ (1.42)	2	20	6	300	90	89:11	40
	SiI· AlClE ₂ (0.33)	5	20	3	2880	44	91:9	41
2b	AlI· AlClE ₂ (1.42)	2	20	1	30	70	92:8	36
	AlI· TiCl ₄ (1.42)	2	-50	2	120	89	92:8	36
	AlI· TiCl ₄ (1.42)	2	-15	3	1440	95	96:4	40
	SiI· AlClE ₂ (0.60)	5	-15	3	150	24	84:16	10
	AlI· TiCl ₄ (1.42)	2	20	3	105	99	89:11	17
2c	AlI· AlClE ₂ (0.60)	5	-15	3	100	15	84:16	14
	AlI· TiCl ₄ (0.60)	5	20	2	120	93	94:6	30
	AlI· TiCl ₄ (0.60)	5	-25	3	1440	35	92:8	33
	AlI· TiCl ₄ (0.60)	5	20	2	30	95	94:6	39
	SiI· AlClE ₂ (0.25)	2.5	-50	3	180	85	85:15	55
SiI· TiCl ₄ (0.25)	2.5	20	3	30	69	85:15	44	
			20	3	120	90	89:11	23
			20	3	120	77	86:14	5

^a Determined by GC (methods for 2a and 2b previously described in refs.9 and 10, respectively). For 2c the following procedure is used: cross-linked methyl silicone column 25x0.2x0.33µm, helium as carrier gas 20 psi, inj. temp. 230°C, det. temp. 250°C, oven temp. program 150°C (4 min) - 2.5°C/min - 175°C, retention times: 2c (2.9 min), 3x (10.8 min), 4x (10.9 min), 3n+4n (11.2 min) b 2a (ref. 9) and 2c determined by GC, 2b determined by ¹H-NMR (ref. 10) c 2a determined by GC (ref. 9), 4n is preferably obtained, 2b determined by ¹H-NMR (ref. 10), 3n is preferably obtained; 2c determined by HPLC: silica porasil 10 µm, 8 mm x 100 mm, detection UV at 210 nm, hexane:THF lineal gradient from 98:2 (2.5 min) to 99:1 (5 min) as mobile phase (3 ml/min), retention times: 3.2 and 3.4 min (3x+4x), 3.9 min (3n), 4.6 min (4n), 3n is preferably obtained.

using silica-modified catalysts, are comparable to those obtained in AlClEt_2 -catalysed reactions, which rules out the formation of **2b**-Ti chelate complexes. Therefore, the extension and direction of the asymmetric induction can be explained by the previously described non-chelate model.¹⁰

The Diels-Alder reaction between **2c** and cyclopentadiene has been studied¹² in the absence of a catalyst, and using several Lewis acids as catalysts. If the asymmetric inductions obtained are considered, $\text{Si1} \cdot \text{AlClEt}_2$ is similar to homogeneous aluminium Lewis acids, whereas $\text{Si1} \cdot \text{TiCl}_4$ resembles ZrCl_4 . Therefore, the formation of **2c**-catalyst chelate complexes can be again ruled out.

To summarise, Lewis acid modified silicas are the most efficient heterogeneous catalysts described to date for Diels-Alder reactions of chiral acrylates. They allow us to obtain diastereomeric excesses similar to those obtained using aluminium homogeneous catalysts. Whereas $\text{Si1} \cdot \text{AlClEt}_2$ is the best catalyst for the reactions of **2a** and **2c**, $\text{Si1} \cdot \text{TiCl}_4$ is more suitable for the reactions of **2b**.

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