

A Study of the Diastereoselectivity of Diels-Alder Reactions on the Ce-SiO₂ as Support

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The diastereoselectivity of Diels-Alder reactions were studied on the silica surface supported with different concentrations of cerium ion as efficient Lewis acid catalysts under solvent-free conditions. The results showed that the diastereoselectivity of reaction was highly improved in these conditions. The cerium ion was grafted on silica surface by using ion exchange method.

Key Words : Diels-Alder (DA), Silica support, Cerium, Cyclopentadiene, Methylacrylate

Diels-Alder (DA) reaction, leading to six membered ring products with controlled regioselectivity and stereochemistry, is a powerful tool in organic synthesis.¹⁻⁴ Lewis acid catalysts, such as ZnCl₂, AlCl₃, FeCl₃, Yb(OTf)₃, and UI₃, can have a significant effect on the rate and *endo* selectivity of DA reactions, especially when they are coordinated to the heteroatom of dienophile, such as the oxygen of carbonyl group.⁵⁻⁷ The carbonyl group become more electron-withdrawing when there is the interaction of metal ions as Lewis acid sites with carbonyl group of dienophile. This effect decreases the energy level of the LUMO of dienophiles and allows more efficiently overlapping with HOMO of the diene.⁸ Therefore, the reaction proceeds with great ease.

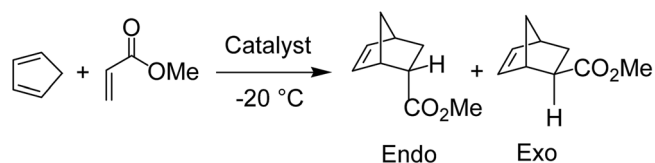
According to the Pearson's HSAB classification, trivalent state of rare earths which located between Mg²⁺ and Ti⁴⁺ are hard acids.⁹ The rare earths salts of strong acids are sometimes able to work as effective Lewis acid catalysts in the presence of water, alcohols, or even amines, although most traditional Lewis acids lose their activities under such conditions.¹⁰ The rare earth Lewis acid could be recovered after reactions and reused without any loss of activity because of their stability. Another important aspect of rare earths is their high coordination numbers. These properties are highly advantageous for coordinating various chiral and achiral ligands around the metal ions and strong affinities to the oxygen of carbonyl group as a hard ligand. Recently, it was reported that chiral rare earth organophosphates-cerium complexes were evaluated as a homogeneous Lewis acid catalyst for the asymmetric hetero-DA reaction.¹¹

Homogeneous Lewis acids have serious drawbacks such as the use of more than one molar equivalent, laborious work-up procedures and problems with environmentally hazardous waste-streams. It was reported that several inorganic solid acids, such as zeolite, clays, mesoporous molecular sieves (Al-HMS and La-SBA-15), alumina, and metal functionalized silica (ZnCl₂, AlCl₃, FeCl₃) are efficient heterogeneous catalysts in DA reactions of Cyclopentadiene.¹²⁻¹⁸

It was proved that silica gel in comparing to the other inorganic material, is a suitable support for the heterogenization of several kinds of catalysts, because it is an abundant

and cheap material, with good adsorption properties due to their high surface area, nanoporousity, and physico-chemical stabilities during the reaction process.¹⁹ The silica surface has two types of functional groups such as siloxane (Si-O-Si) and silanol group (Si-OH). Silanol groups on silica surface behave like a weak acid (pK_a = 9.4), thus they have both strong hydrogen bonding and dipole-dipole interactions as the well known Brønsted acid.^{20,21} The acidity of surface was obtained and changed by adding a metal ion on the surface by increasing metal charge and concentration.^{22a}

In this work, the various concentrations of Lewis acid on silica gel surface were obtained by using ion exchange method of cerium ion (III) and (IV) in alkali conditions.^{22b} Then, the diastereoselectivity of DA reactions of cyclopentadiene and methylacrylate with the resulting solid acids in the absence of solvent were studied. The high *endo/exo* diastereoselectivity was observed for more charge and high concentration of cerium ion on silica surface.



Results and Discussion

The results of the Diels-Alder reactions between cyclopentadiene and different methylacrylate in the presence of various prepared supports (so-called X-A-Ce-SiO₂ which correspond to the preparation of supports with various concentrations of cerium solution in molar unit (X = 0.05 M to 0.08 M) and oxidation state of cerium ion (A = 3 and 4)) are summarized in the Tables 1 and 2. For pure silica as support, 0-A-Ce-SiO₂, the reaction exhibits good yield, but less and poor diastereoselectivity of reaction. The yield and specially diastereoselectivity increase in the case of support with high concentration of cerium ion on silica surface as the results shown in the Table 1 and 2. By the GC-Mass results for this diene, it was shown that the product which was passed from column at 6.048 min is the main reaction

Table 1. Diastereoselectivity and yield of Diels-Alder reaction of methylacrylate and cyclopentadiene using Ce (III) loaded on silica as support

Concentration of Ce(III), (X-3-Ce-SiO ₂) ^a	mmol Ce/g Silica ^b	yield (%)	de (%)	endo/exo
Without support	–	98	55	77:23
SiO ₂	0	92	67	83:17
0.05 -3-Ce-SiO ₂	0.25	96	85	92:8
0.06 -3-Ce-SiO ₂	0.3	95	86	93:7
0.07 -3-Ce-SiO ₂	0.35	97	88	94:6
0.08 -3-Ce-SiO ₂	0.4	97	90	94:4

^aThe X-3-Ce-SiO₂ correspond to the preparation of supports with various concentrations of cerium solution in molar unit (X = 0.05 M to 0.08 M) and oxidation state of cerium ion is 3. ^bThe amount of cerium ion loaded on silica was determined by ICP method.

Table 2. Diastereoselectivity and yield of Diels-Alder reaction of methylacrylate and cyclopentadiene in the presence of Ce (IV) loaded on silica as support

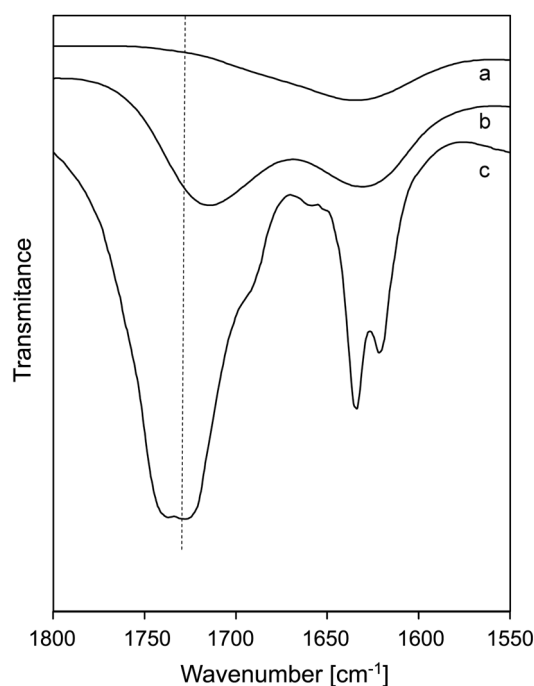
Concentration of Ce(IV), (X-4-Ce-SiO ₂) ^a	mmol Ce/g Silica	yield (%)	de (%)	endo/exo
Without solvent	–	98	55	77:23
SiO ₂	0	92	67	83:17
0.05 -4-Ce-SiO ₂	0.25	96	89	93:7
0.06 -4-Ce-SiO ₂	0.3	97	92	96:4
0.07 -4-Ce-SiO ₂	0.35	99	93	97:3
0.08 -4-Ce-SiO ₂	0.40	99	94	98:2

^aThe X-4-Ce-SiO₂ corresponding to the preparation of supports with various concentrations of cerium solution in molar unit (X = 0.05 M to 0.08 M) and oxidation state of cerium ion is 4.

product and the m/e at 152 and 66 respectively are concerned to parent and base peak.

As mentioned above, when the concentration of metal ion on surface is increased, the Lewis acid sites of cerium ion on the surface of silica will be increased. Thus, with the high cerium ion concentration on the silica surface, the diastereoselectivity of reaction will be increased. Because of the limited capacity of silica for grafting the cerium ion, by increasing of cerium ion concentration to 0.2 M, the ICP results showed the exist of cerium ion in the filtered solution, furthermore the diastereoselectivity did not improved more than of 24% so the concentration study was stopped till 0.2 M. On the other hand, the *endo/exo* diastereoselectivity and yield for Ce(IV) are rarely higher than Ce(III), which may be due to its relative strong acidic properties.

The FT-IR spectra of the Ce(IV) modified silica, free methylacrylate, and the loaded methylacrylate on the Ce(IV) modified silica were shown in the Figure 1. The symmetry stretching frequency of C=O for free methylacrylate is observed at 1730 cm⁻¹. When, methylacrylate is loaded on the Ce(IV) modified silica, the carbonyl frequency shifts about 20 cm⁻¹ to the low wave number region. This frequency shift of C=O to low wave number is attributed to the coordination of methylacrylate with cerium ions on the silica surface. It was reported that this band shifted to the low wave number region about 10 cm⁻¹, when the metal ion was Zn(II).²³ Cerium (IV) is a strong Lewis acid than Zn(II), thus

**Figure 1.** FTIR spectra of a) 0.08-4-Ce-SiO₂, b) loaded methylacrylate on 0.08-4-Ce-SiO₂, c) methylacrylate.

the frequency shift of C=O for cerium ion will shift to the lower wave number region than zinc ion. However, the width of this band is attributed to the several kinds of carbonyl groups coordination and also possibility of hydrogen bonding with the Si-OH of silica surface. The spectrum of Ce(IV) modified silica (Fig. 1a) is presented only for comparing.

The exact mechanism of these metal functionalized silica effects is not well understood.²³ Vesselovskii and coworker have proposed that the adsorption of reactants on the surface of silica particles may facilitate the formation and stabilization of pre-reaction complexes by bringing the reacting moieties within each reactant into closer proximity.²⁴ A related theory has been advanced by Menger who suggested that the rigid anchoring of functional groups can fix reactants in proximity to each other less than the critical bonding distance, thus leading to significant rate enhancements.²⁵ An alternative theory introduced by Parlar and Baumann²⁶ who suggested that only a small fraction of reactants are actually strongly adsorbed on the silica surface and that the enhanced rates and selectivities are caused by symmetry controlled secondary orbital interactions between strongly adsorbed species and species that are free to move about on the surface. Previous theories to account for the promotion of reactions on the surface of silica were developed for processes taking place in the absence of solvent.⁸ However, the catalytic mechanism in this work is proposed by the adsorption and coordination of Lewis acid site of cerium ion with the carbonyl of methylacrylate and probably hydrogen bonding or protonation of the dienophile by acidic SiOH groups on the silica surface and then the DA reaction carries out with facility.

Table 3. Diastereoselectivity and yield of Diels-Alder reaction of cyclopentadiene with other dienophiles in the presence of Ce(IV) loaded on silica as support

Diene	yield (%)	de (%)	endo/exo
methyl methacrylate	79	89	93:17
methylacrylate	99	94	98:2
methylvinylketone	85	93	97:3
crotonaldehyde	77	68	84:16
ethylvinylether	–	–	–

Table 4. Diastereoselectivity and yield of Diels-Alder reaction of cyclopentadiene with methylacrylate in the presence of recycled Ce(IV) loaded on silica as support

Time	yield (%)	de (%)	endo/exo
first	99	94	98:2
second	96	90	96:4
third	94	90	96:4
fourth	94	90	96:4

Finally, we have decided to develop the reaction of cyclopentadiene with the other dienophiles under the solvent free conditions using X-A-Ce-SiO₂ as support. The results which obtained by GC-Mass analysis, were shown in Table 3. As you see, the best results for diastereoselectivity are concerned to use methylacrylate and methylvinylketone as dienophile.

We continued the reaction with methylacrylate as dienophile and 0.08-4-Ce-SiO₂ as support (Table 2). After the period of reaction, the support was recycled and reused for 4 times. For each time, the results of yield and Diastereoselectivity were calculated by the GC and GC-Mass analysis as shown in the Table 4. As these results, we see that this support could be recycled and reused for several times. The diastereoselectivity of blank reaction without support and solvent was 55%. The reaction in solvent without support had diastereoselectivity of 56% so the solvent does not have any effect on improving the diastereoselectivity. For proving that the reaction was completed before the extraction step with Soxhlet, in other tray, the extraction was done just by filtering the product from the catalyst and the GC results showed the same diastereoselectivity. Therefore before the extraction step, the reaction was completed.

Conclusions

The cerium ion on silica surface catalysts prepared by using ion exchange method were proved to be effective heterogeneous catalysts for high diastereoselective DA reaction of cyclopentadiene and dienophiles without solvent. The diastereoselectivity of the reaction strongly depends on the concentration and charge of cerium ion as a hard Lewis acid on the silica surface. There is a direct relation between concentration and charge of cerium ion on the silica surface and diastereoselectivity of DA reaction. The characteristic FT-IR band for C=O stretching frequency indicated that

methylacrylate was coordinated with cerium ions on the surface of silica. The catalytic mechanism was suggested by adsorption and the carbonyl group coordination of methylacrylate with cerium ion on the silica surface which have a great role in the diastereoselectivity of DA reactions.

Experimental Section

Materials and methods. Ce(NO₃)₃·6H₂O or Ce(SO₄)₂·4H₂O, ammonium solution, dicyclopentadiene, silica (kieselgel 60, particle size 63-200 μm, S_{BET} = 450 m²/g) were purchased from Merck company. Acetone and methylacrylate was purchased from Merck and were freshly distilled before use. Cyclopentadiene was freshly prepared by pyrolysis of dicyclopentadiene at 170 °C for each reaction and keep at –20 °C. Gas chromatography was performed with a gas chromatograph with HP-5 column, 5% Phenyl Methyl Siloxan capillary (30 m × 530 μm × 1.50 μm). Infrared spectra were collected on a Bruker TENSOR 27 FT-IR spectrophotometer.

Preparation of supports. Silica gel (20 g) was added to ammonium solution 1 M for 5 min. To the obtained NH₄⁺-SiO₂, the solution of Ce(NO₃)₃·6H₂O and Ce(SO₄)₂·4H₂O with various concentration 0.05 to 0.08 M was added with stirring for 1 h in room temperature. At this time, the ion-exchange between NH₄⁺ and cerium ion takes place. The solids were filtered and washed with 30 mL acetone and then dried in oven for 2 h. Next, for removal of none ion-exchanged NH₄⁺ and reducing the silanol of surface, all solids were heated at 350 °C under vacuum for 2 h. All obtained solids were stored in polypropylene bottle until used as support. The index X-A-Ce-SiO₂ corresponding to the preparation of supports with various concentrations of cerium solution in molar unit (X = 0.05 M to 0.08 M) and oxidation state of cerium ion (A = 3 and 4).

X-A-Ce-SiO₂ DA reaction under solvent-free conditions (in a phase of gel). Methylacrylate (0.9 mL, 10 mmol) was added to 0.08-4-Ce-SiO₂ (5 g, 2 mmol Ce/5 g SiO₂) as support in very small portion with vigorous stirring of solid in a stopped flask. The reaction mixture was stirred for 30 min and cooled about –20 °C, then freshly distilled cyclopentadiene (2.5 mL, 26 mmol) was added to this mixture with vigorous stirring. It was stirred for 2 h at –20 °C. Finally, the crude product was extracted with acetone or methanol in a Soxhlet about 24 h. The yield of reaction was determined by GC with an standard solution of methylacrylate in dichloromethane. The endo/exo ratio was 98:2. The GC-Mass data was shown two peaks in m/e 152 and 66 ascribed to parent and base peaks, respectively. The same reactions were done for the other catalysts.

For comparing, this reaction was carried out with any catalyst in acetone and dichloromethane as solvent and also the other tray was done without any solvent and catalyst too.

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References

1. Fringuelli, F.; Taticchi, A. *Diels-Alder Reaction*; Wiley: New York, 2002.
 2. Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1990.
 3. Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 3, 439.
 4. Kumar, A. *Chem. Rev.* **2001**, 101, 1501.
 5. Yates, P.; Eaton, P. *J. Am. Chem. Soc.* **1960**, 82, 4436.
 6. Inukai, T.; Kojima, T. *J. Org. Chem.* **1971**, 36, 924.
 7. Alves, C. N.; da Silva, A. B. F.; Marti, S.; Moliner, V.; Oliva, M.; Andres, J.; Domingo, L. R. *Tetrahedron* **2002**, 58, 2695.
 8. Weinstein, D.; Rensle, R.; Danheiser, L.; Tester, W. *J. Phys. Chem.* **1999**, B103, 2876.
 9. Pearson, R. G. *Hard and Soft Acids and Bases*; Hutchinson & Ross: Stroudsburg, 1973.
 10. Kobayashi, S.; Nagayama, S.; Busujima, T. *J. Am. Chem. Soc.* **1998**, 120, 8287.
 11. Furuno, H.; Hayano, T.; Kambara, T.; Sugimoto, Y.; Hanamoto, T.; Tanaka, Y.; Zhi Jin, Y.; Hagawa, T.; Inanaga, J. *Tetrahedron* **2003**, 59, 10509.
 12. Mahmoudi Najafi, H.; Gandi, M.; Farzaneh, F. *Chem. Lett.* **2000**, 358.
 13. Liu, J.; Yin, D.; Yin, D.; Fu, Z.; Li, Q.; Lu, G. *J. Mol. Catal.* **2004**, A209, 171.
 14. Onka, M.; Hashimoto, N.; Yamasaki, R.; Kibata, Y. *Chem. Lett.* **2002**, 166.
 15. Onka, M.; Hashimoto, N.; Kibata, Y.; Yamasaki, R. *Appl. Catal.* **2003**, A241, 307.
 16. Sreekanth, P.; Kim, S.; Hyeon, T.; Kima, B. M. *Adv. Synth. Catal.* **2003**, 345, 936.
 17. Fraile, J. M.; Garcia, J.; Mayoral, J. A.; Grazia Proietti, M.; Sanchez, M. C. *J. Phys. Chem.* **1996**, 100, 19484.
 18. Chavan, S. P.; Sharma, A. K. *Synlett* **2001**, 5, 667.
 19. Clark, J. H. *Supported Reagents in Organic Reactions*; VCH: Weinheim, 1994.
 20. Iler, R. K. *The Chemistry of Silica, Solubility, Polymerization, Colloid and Surface Properties, and Biochemistry*; John Wiley & Sons: New York, 1979.
 21. Badii, A.; Mohammadi Ziarani, G.; Norouzi, P.; Tousi, F. *Iranian International J. Sci.* **2004**, 5, 31.
 22. (a) Che, M.; Bonneviot, L. *Pure Appl. Chem.* **1988**, 60, 1369. (b) Cho, I.; Ahn, K.-D. *Journal of the Korean Chemical Society* **1976**, 20, 299.
 23. Veselovsky, V. V.; Lozanova, S. A. L.; Moiseenkov, A. M.; Smith, W. A.; Caple, R. *Tetrahedron Letters* **1988**, 29, 175.
 24. Veselovskii, V. V.; Gybin, A. S.; Lozanova, A. V.; Moiseenko, A. M.; Smith, W. A. *Bull. Acad. Sci. USSR* **1990**, 107.
 25. Menger, F. M. *Acc. Chem. Res.* **1985**, 18, 128.
 26. Parlar, H.; Baumann, R. *Angew. Chem., Int. Ed. Engl.* **1981**, 20, 1014.
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