Magnesium-Lanthanum Mixed Metal Oxide: a Strong Solid Base for the Michael Addition Reaction

Bhaskar Veldurthy, Jean Marc Clacens, François Figueras*

Institut de Recherches sur la Catalyse du CNRS, 2 Av. A. Einstein, 69626 Villeurbanne Cedex, France
Fax: (+33)-6221-487-672, e-mail: figueras@catalyse.cnrs.fr

Received: December 6, 2004; Accepted: March 7, 2005

Abstract: Michael additions were achieved quantitatively at room temperature with a broad spectrum of acceptors and donors, using a magnesium-lanthanum mixed oxide, a strong solid base. The best solvent for the reaction is dimethylformamide, but good yields were also obtained using toluene as solvent. The results obtained with magnesium-lanthanum are comparable to those reported for super bases. The catalyst can be separated from the reaction mixture and recycled five times without loss of activity with no other treatment.

Keywords: basic catalysis; magnesium-lanthanum mixed oxide; Michael additions; recyclability; solvent effects

The Michael addition is a reaction for C–C bond formation, involving the nucleophilic addition of a carbanion to α,β-unsaturated carbonyl compounds and is therefore base-catalysed. This reaction has found multiple industrial applications for the production of monomers,[1,2] corrosion inhibitors,[3] coatings,[4] and pharmaceuticals.[5] This reaction is industrially catalysed by liquid bases such as alkoxides, tertiary amines, non-ionic bases,[6,7] and superbases such as proazaphosphatranes.[8–10] A variety of solid bases has also been described including barium hydroxide,[11] KF supported on γ-Al_2O_3,[12] α-Al_2O_3,[13] phosphates,[14,15] on hydrotalcites,[16,17] amines anchored at surfaces,[18] and organic resins.[19] Most of these solids are weak bases which are effective only with a restricted class of electrophilic olefins such as α,β-unsaturated esters or conjugated enones. Recycling of the catalyst has seldom been demonstrated except for KF/natural phosphate which can be recycled after calcination at 973 K, which represents a severe limitation to its practical use.

We report here the properties of Mg-La mixed oxides for different Michael additions. This catalyst has been recently used for the transesterification of diethyl carbonate by alcohols.[20] A comparison of substrates with different pK_a allows us to estimate the possibilities of the catalyst and also gives an evaluation of the basic strength at the surface.[21] We used here donors with pK_a values, measured in DMSO,[22] varying from 8 for thiocresol to 16.4 for diethyl malonate and 17.2 for nitromethane.

The Mg-La mixed oxide was obtained by co-precipitation of Mg and La nitrates (0.386 and 0.129 mol, in water 0.5 L, for an atomic ratio Mg/La = 3) at a constant pH = 10 using a mixture of KOH (1 mol) and K_2CO_3 (0.26 mol) in 0.52 L of distilled water. The samples (about 0.15 g) were activated at 923 K in an air flow, using a temperature ramp of 10 K/min. Just before use, they were reactivated at 773 K in air and not rehydrated.

The chemical analyses of the solid catalyst give the composition: La: 39.8%; K: 5.4%; H_2O: 37%. The Mg/La ratio in the solid is then 4.26, compared to 3 in the solution, therefore the precipitation of La is not complete at pH 10. The powder XRD pattern of the uncalcined Mg-La mixed oxide contains diffraction lines of a hydrated lanthanum carbonate as well as magnesium and lanthanum hydroxides. This triphasic solid probably consists of a layer of lanthanum oxide deposited on magnesia.

The surface area of this mixed oxide is 37.6 m^2/g after calcination at 923 K, and supporting La on magnesia thus renders the surface area stable. The enthalpy of adsorption of CO_2 as measured by microcalorimetry allows us to evaluate the basic strength of the solid, and the number of basic sites is then measured by the amount adsorbed. The results are reported in Figure 1. Mg-La mixed oxide decarbonated at 673 K is a strong base, adsorbing about 10 μmol/g of CO_2 with an enthalpy > 140 kJ/mol. This base strength is significantly higher than that of KF supported on γ- or α-Al_2O_3, for which enthalpies of adsorption below 120 kJ/mol have been determined. Calcined, then hydrated hydrotalcite (HDT-OH) investigated earlier adsorbed about 0.25 mmol/g with a constant heat of adsorption of 100 kJ/mol,[23] so Mg-La mixed oxide appears to be a stronger base with a smaller number of sites.

The results obtained for the reaction of *trans*-chalcone on different donors are reported in Table 1. The observation of fast reactions at room temperature demonstrates that MgLa has sites able to abstract a proton from reactants of high pK_a, and possesses a corresponding high basic strength. Quantitative yields are observed with different Michael donors. Recycling of the catalyst

DOI: 10.1002/adsc.200404371

was investigated with ethyl cyanoacetate and chalcone, pumping out the reaction medium with a syringe and adding new reactants. The catalyst can be recycled 5 times with no loss of activity (Table 1, entry 2), and without any temperature treatment. The catalyst is then reusable after no special treatment.

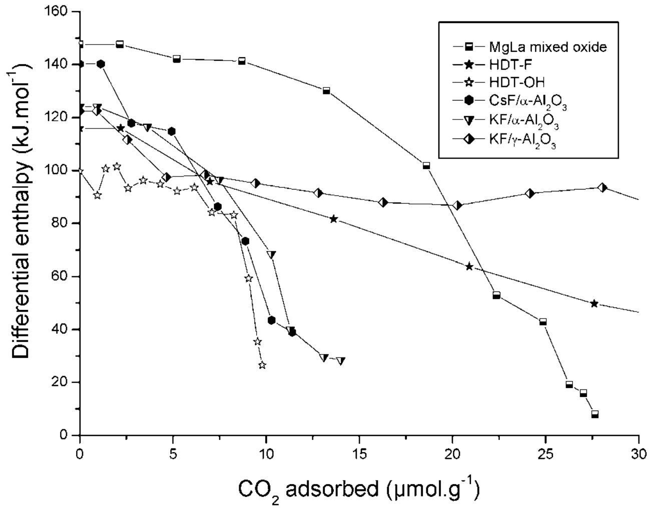
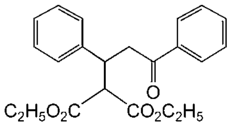
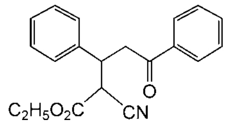
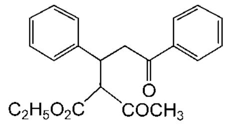
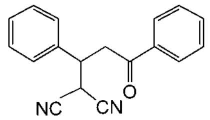
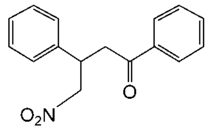


Figure 1. Basicity, measured by CO_2 adsorption of the catalysts used for Michael condensation.

The reaction is also fast and selective with many acceptors as illustrated in Table 2. The yield is usually quantitative at room temperature, but the reaction of hexyl acrylate on nitroethane requires 313 K and on diethyl malonate 353 K. It is interesting to notice that pure La_2O_3 was found to be inactive for the Michael addition of nitromethane on cyclohexenone at 323 K,[24] so that the mixed oxide appears much more active. Anchored quaternary amines also give either poor activity or poor selectivity to Michael adducts in the reactions of ethyl cyanoacetate with cyclohexenone and methyl vinyl ketone.[25] The present catalyst is also more active than KF/natural phosphate for the reaction of nitromethane on chalcone, achieved quantitatively with the mixed oxide in 2 h and only with 60% yield in 6 h on supported KF.[14] The high reactivity of nitromethane at room temperature on the mixed oxide proves that this solid possesses strong basic sites.

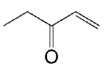
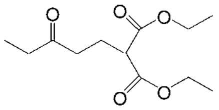
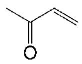
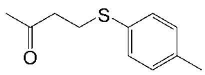
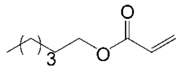
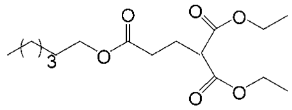
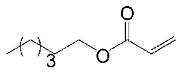
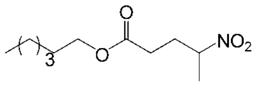
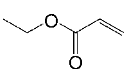
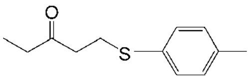
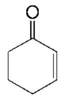
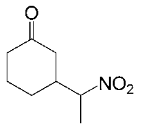
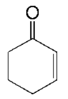
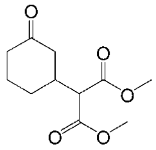
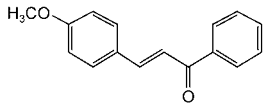
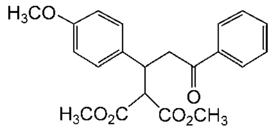
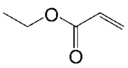
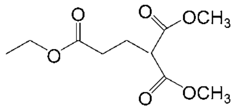
The results obtained with Mg-La mixed oxide are compared in Table 3 to those reported for some other solid bases. Potassium fluorides supported on α-alumina give good results with a 1/1 ratio of reactants, but due to their lower basic strength have to be operated at 323 K. CsF/ α-Al_2O_3 shows a higher activity also consistent with a higher initial enthalpy of CO_2 adsorption. The catalytic activity measured by the time required to reach complete conversion for the room temperature Michael ad-

Table 1. Michael addition of active methylene compounds with *trans*-chalcone catalysed by Mg-La mixed oxides, using an acceptor/donor ratio of 1:1.1, and DMF as solvent at room temperature under a nitrogen atmosphere

Entry	Donor	pK_a in DMSO	Product	Reaction time [h]	Yields[a] [%]
1	diethyl malonate	16.4		5.5	98
2	ethyl cyanoacetate	13.1		1.5	97, 98[b]
3	ethyl acetoacetate	14.2		1	82[c]
4	malononitrile	11.1		0.16	99
5	nitromethane	17.2		2	98

[a] Yield of isolated products.
[b] 5th recycle.
[c] Reaction performed at 333 K.

Table 2. Comparison of different acceptors for Michael condensations at 298 K using an acceptor:donor ratio of 1:1.1.

Acceptor	Donor	Product	Reaction time [h]	Yield [%][a]
	diethyl malonate		3.0	98
	*p*-thiocresol		0.45, 0.50	97, 96[b]
	diethyl malonate		3.5, 0.45[c]	99, 97
	nitroethane		3.5[d]	98[c]
	*p*-thiocresol		1.0	98
	nitroethane		0.25	99
	dimethyl malonate		4.0	98
	dimethyl malonate		4.5	78[e]
	dimethyl malonate		5.0, 5.5	96, 97[b]

[a] Yield of isolated products.
[b] 5th recycling of the catalyst.
[c] Reaction performed at 353 K.
[d] Reaction performed at 313 K.
[e] The remainder is the unreacted substrates.

dition of nitroethane on cyclohexenone is consistent with the basic strengths determined by calorimetry. On the two reactions of diethyl malonate with chalcone and methyl vinyl ketone, Mg-La is not more active than fluorinated hydrotalcite but reaches a higher yield, suggesting that the inhibition by the products is lower. The inhibition by the products was earlier proposed to explain the lower reaction rate on KF/α-alumina in the absence of solvent.[13] From a synthetic point of view it is, however, interesting to work in concentrated media, and the catalytic properties reported here for Mg-La are probably underestimated. The low activity of supported quaternary amines,[25] can also be a result of a high concentration.

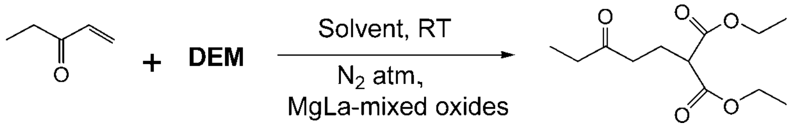
It is interesting to compare these results with those reported recently by Kisanga et al.[9] for Michael additions, using the superbase $P(RNCH_2CH_2)_3N$ as catalyst. This catalyst catalyses the reaction of 2-cyclohexenone (2.1 mmol) with nitromethane or nitropropane (2 mmol) at room temperature in about 0.5 h using 10% of base, and isobutyronitrile as solvent. The turnover which can be then calculated is 20 mol per mol catalyst per hour. For the reaction of nitroethane on cyclohexenone, taking into account that on Mg-La mixed oxide, the number of strong basic sites is about 20 $\mu mol \cdot g^{-1}$, the turnover would be 400 $mol \cdot mol^{-1}\,h^{-1}$. Indeed part of the difference is accounted for by the higher reactivity of nitroethane compared to nitromethane, however, us-

Table 3. Time and temperatures required for a given conversion for different solid bases.

Michael acceptor	Michael donor	Catalyst	Temp. [K]	Time [h]	Yield [%]	Ref.
Chalcone	Diethyl malonate	HDT-OH[a]	298	6	96	[28]
		HDT-F[b]	298	2	95	[29]
		HDT-O-*t*-Bu[c]	298	2	95	[17]
		Mg-La oxide	298	5.5	98	
Methyl vinyl ketone	Diethyl malonate	Mg-La	298	3	98	
		HDT-F[b]	298	2	80	[29]
		NR_4/MCM-41[d]	333	2	10	[25]
Cyclohexenone	Nitroethane	HDT-F	298	1.5	98	[29]
		HDT-O-*t*-Bu	298	0.5	98	[17]
		Mg-La	298	0.25	99	
		KF/α-Al_2O_3[e]	323	5	85	[13]
		KF/γ-Al_2O_3[e]	323	8	39	[13]
		CsF/α-Al_2O_3[e]	323	0.75	90	[30]

Reaction conditions:
[a] Acceptor (2 mmol), donor (2 mmol), catalyst (1 g) in 10 mL *n*-hexane.
[b] Acceptor (1 mmol), donor (1 mmol), catalyst (0.1 g), in 5 mL CH_3CN.
[a] Acceptor (2 mmol), donor (2 mmol), catalyst (0.1 g), in 10 mL CH_3OH.
[d] Acceptor (8 mmol), donor (8 mmol); catalyst (0.060 g), in 2 mL CH_3CN.
[e] Acceptor (1 mmol), donor (1 mmol), catalyst (0.1 g), in 10 mL DMF.

Table 4. Solvent effect on Michael addition.



Entry	Solvent	Reaction time [h]	Isolated Yield [%]
1	Toluene	12	81
2	THF	12	78
3	DMF	3	98
4	MeOH	6	Non-Michael adduct

ing KF/ α-Al_2O_3 as catalyst,[13] nitromethane was found to be only two times less reactive than nitroethane. Therefore the activity of the mixed oxide is of the same magnitude as that of the superbase for this type of reaction, in DMF as solvent.

N-Phenyl-tris(dimethylamino)iminophosphorane immobilized on polystyrene resin (P-BEMP) has been recently reported[6] to catalyze, at room temperature, Michael additions of 1,3-dicarbonyls with various acceptors. This organic catalyst was used in THF or alcohols, with a mixture of carbonyl compound (2 mmol) and Michael acceptor (2.2 mmol) in 8 mL of solvent and P-BEMP (5 mol %). Since the reaction conditions and the substrates are different, it is more difficult to compare this catalyst with Mg-La mixed oxide. However, it can be remarked that the pK_a of the donors is lower (about 10–15 in DMSO), which should correspond to a higher reactivity. However, reaction times reach 4 to 72 h, suggesting a lower activity of the organic catalyst compared to the Mg-La mixed oxide. In recycling experiments using these conditions, the reaction time increases from 4 to 16 h, suggesting deactivation. A good stability could be obtained using a mixture of 1,3-dicarbonyl (0.5 mmol) and Michael acceptor (1 mmol) in 3 mL solvent and P-BEMP (5 mol %), but this excess of acceptor would imply to a large recycling of reactant.

An important point in practice is the choice of a solvent, since not all can be used on the industrial scale. The effect of the solvent was investigated using the reaction of ethyl vinyl ketone with diethyl malonate. From the results, reported in Table 4, it appears that the best solvent would be DMF, which was also found to be the best solvent for aldolisation.[26] Methanol was a poor solvent for the Michael addition and promoted an unidentified side reaction. THF and especially toluene were nearly equivalent and could be good compromises for industrial applications.

In conclusion, the present results prove that Mg-La mixed oxides calcined at 823 K are solid bases of strong basicity, able to activate nitromethane and diethyl malonate at room temperature, and showing the ability to work well in relatively concentrated solutions in toluene. In the conditions used here the catalyst can be recycled several times without any thermal treatment. Since the preparation of this solid includes a calcination at 923 K it could be regenerated at high temperature by oxidation of deposited heavy organics in the case of a possible contamination. This is not possible for organic catalysts.

Experimental Section

Catalyst Characterization

The solids were analysed by ICP after dissolution by acid attack. The surface areas were determined from the isotherms of adsorption of N_2 at 77 K using the BET equation. X-Ray powder diffraction patterns were recorded on a Phillips instrument using CuKα1 radiation. The isotherm for N_2 adsorption at 77 K was determined on solids activated at 723 K in N_2 or air, then desorbed *in situ* at 473 K in vacuum. Basicities were characterised by microcalorimetry using CO_2 adsorption at 303 K with a Tian-Calvet calorimeter on samples activated in vacuum at 673 K.[27]

Catalytic Tests

The reactions were performed at room temperature in different solvents, using typically 2 mmol of each reactant and 4 mL of solvent with 0.1 g of solid catalyst calcined at 773 K. The products were separated at the end of the reaction and characterised by NMR and GC-MS. The reaction usually gives a single product, with no other side reaction such as Knoevenagel condensation. The conversion was estimated from the changes in the amount of substrate.

Acknowledgements

Thanks are due to the technical services of IRC for their help in catalyst characterization.

References

[1] R. J. Clemens, (Eastman Kodak Co., USA), *US Patent* 5,017,649, **1991**.

[2] N. Nakamura, K. Shigemori, T. Otsuki, Y. Mashimo, M. Kawashima, A. Ikeda, T. Sato, H. Saito, (Toyo Ink Manufacturing Co., Ltd., Japan), *Patent* WO 0116203, **2001**.

[3] G. R. Meyer, (Nalco/Exxon Energy Chemicals, L. P., USA), *US Patent* 5,993,693, **1999**.

[4] A. Noomen, *Progress in Organic Coatings*, **1997**, *32*, 137–142.

[5] E. J. Hessler, S. I. Amin, (Upjohn Co., USA), *European Patent* EP0022440, **1981**.

[6] D. Bensa, T. Constantieux, J. Rodriguez, *Synthesis* **2004**, 923–927.

[7] D. Bensa, J. Rodriguez, *Synth. Commun.* **2004**, *34*, 1515–1533.

[8] P. B. Kisanga, J. G. Verkade, *Tetrahedron* **2001**, *57*, 467–475.

[9] P. B. Kisanga, P. Ilankumaran, B. M. Fetterly, J. G. Verkade, *J. Org. Chem.* **2002**, *67*, 3555–3560.

[10] A. E. Wroblewski, V. Bansal, P. Kisanga, J. G. Verkade, *Tetrahedron* **2003**, *59*, 561–566.

[11] A. Garcia-Raso, J. Garcia-Raso, B. Campaner, R. Mestres, J. V. Sinisterra, *Synthesis* **1982**, 1037–1041.

[12] J. H. Clark, D. G. Cork, M. S. Robertson, *Chem. Lett.* **1983**, 1145–1148.

[13] J.-M. Clacens, D. Genuit, L. Delmotte, A. Garcia-Ruiz, G. Bergeret, R. Montiel, J. Lopez, F. Figueras, *J. Catal.* **2004**, *221*, 483–490.

[14] M. Zahouily, B. Bahlaouan, M. Aadil, A. Rayadh, S. Sebti, *Organic Process Research and Development* **2004**, *8*, 275–278.

[15] M. Zahouily, Y. Abrouki, A. Rayadh, S. Sebti, H. Dhimane, M. David, *Tetrahedron Lett.* **2003**, *44*, 2463–2465.

[16] B. M. Choudary, B. Kavita, N. S. Chowdari, B. Sreedhar, M. L. Kantam, *Catalysis Lett.* **2002**, *78*, 373–377.

[17] B. M. Choudary, M. Lakshmi Kantam, B. Kavita, C. Venkat Reddy, F. Figueras, *Tetrahedron* **2000**, *56*, 9357–9364.

[18] A. Corma, S. Iborra, I. Rodriguez, M. Iglesias, F. Sanchez, *Catalysis Lett.* **2002**, *82*, 237–242.

[19] R. Ballini, P. Marziali, A. Mozzicafreddo, *J. Org. Chem.* **1996**, *61*, 3209–3211.

[20] B. Veldurthy, F. Figueras, *Chem. Commun.* **2004**, *10*, 734–735.

[21] A. Corma, V. Fornes, R. M. Martin-Aranda, H. Garcia, J. Primo, *Appl. Catal.* **1990**, *59*, 237–248.

[22] F. G. Bordwell, *Acc. Chem. Res.* **1988**, *21*, 456–463.

[23] J. Sanchez-Valente, F. Figueras, M. Gravelle, P. Kumbhar, J. Lopez, J.-P. Besse, *J. Catal.* **2000**, *189*, 370–381.

[24] H. Kabashima, H. Tsuji, T. Shibuya, H. Hattori, *J. Mol. Catal. A: Chem.* **2000**, *155*, 23–29.

[25] M. J. Climent, A. Corma, S. Iborra, A. Velty, *J.Mol. Catal. A: Chem.* **2002**, *182–183*, 327–342.

[26] J. Lopez, R. Jacquot, F. Figueras, *Stud. Surf. Sci. Catal.* **2000**, *130A*, 491–496.

[27] P. C. Gravelle, *Adv. Catal.* **1972**, *22*, 191.

[28] B. M. Choudary, M. Lakshmi Kantam, C. R. Venkat Reddy, K. Koteswara Rao, F. Figueras, *J. Mol. Catal. A: Chem.* **1999**, *146*, 279–284.

[29] B. M. Choudary, M. Lakshmi Kantam, V. Neeraja, K. Koteswara Rao, F. Figueras, L. Delmotte, *Green Chem.* **2001**, *3*, 257–260.

[30] J.-M. Clacens, D. Genuit, B. Veldurthy, G. Bergeret, L. Delmotte, A. Garcia-Ruiz, F. Figueras, *Appl. Catal. B: Environmental* **2004**, *53*, 95–100.