Direct Henry reactions with modified calcium oxide as solid catalyst

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Abstract Commercial CaO was modified simply with benzyl bromide. The modified CaO had good water resistance, and characterization by FTIR and TG revealed the modifier was chemically bonded to the CaO surface. Commercial CaO and CaO modified with benzyl bromide were investigated as catalysts for the Henry reaction between benzaldehyde and nitromethane. It was found that the catalytic activity of the modified CaO was greatly improved, with high conversion of benzaldehyde to the (E)-phenyl nitroolefin and 1-phenyl-2-nitroethanol, and with different selectivity from commercial CaO. The effect of modification and reaction conditions on yield, selectivity, and mechanism were studied thoroughly.

Keywords Henry reaction · Heterogeneous catalyst · CaO · Modification

Introduction

The Henry reaction is an important C–C bond-formation reaction producing β nitroalcohol chiral carbon atoms by adding a nitroalkane to a carbonyl compound, for example benzaldehyde. Further reduction of the nitro group of the β -nitroalcohols can lead to the formation of aminoalcohols; this occurs widely with natural and synthetic products and with chemical intermediates [1–3]. Henry reactions with impressively high conversion are realized by use of a variety of homogeneous bases, for example alkali metal oxides, alkaline earth oxides, and hydroxides, which are corrosive, toxic, nonreusable, and also produce neutralization waste [4].

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Ignoring the high cost and rigorous preparation process, the Henry reaction catalyzed by chloroaluminate ionic liquids, especially mixtures of substituted organic species with AlCl₃, results in good yields with efficient recycling [5, 6]. To solve the problem associated with homogeneous bases, several solid bases, for example ion-exchange resin, amorphous silica [7], and zeolite [8] has been reported. Choudary et al. [9] developed efficient Mg-Al hydrotalcite by incorporation of tbutoxide by use of an exchange process to increase the basicity of the hydrotalcite. Nanocrystalline MgO and its modified particles are effective and reusable catalysts for the Henry reaction. However, the nature of the active sites on the modified MgO surfaces is unknown and the catalytic properties of MgO materials depend substantially on the method of preparation [10, 11]. CaO, with strong basicity and low cost, has much potential for catalyzing the Henry reaction. However, this kind of solid base has not been widely used industrially because of the technical problem of the stability of the material on exposure to moist air. The basic sites of alkaline-earth metal oxide or hydrotalcite-like surfaces are easily poisoned by air because of adsorption of CO_2 and H_2O on the surface [12]. Furthermore, for the two-phase reaction with solid catalyst and liquid reactants, the single contact between reagents and catalysts is a major limitation of reaction efficiency, which results in the catalyst being less active than a homogeneous strong base, for example sodium hydroxide.

In this work, commercial CaO was investigated as a catalyst for the Henry reaction of benzaldehyde with nitromethane, and the effects of reaction conditions were investigated. The effects of modification and reaction conditions on yields, selectivity, and mechanism were also studied.

Results and discussion

Catalyst characterization

Modification of CaO by benzyl bromide was as suggested in Scheme 1. IR spectra of commercial CaO and modified CaO are shown in Fig. 1. The spectra contain bands at 867 and 1,477 cm⁻¹ corresponding to vibration modes of mono and bidentate carbonates. It is also apparent from the characteristic absorption of C=O between 2,000 and 1,600 cm⁻¹ that calcium carbonate is present in both catalysts. However, there is no great difference between their intensity, suggesting little carbonation of modified CaO by CO₂ in air. The bands at 1,621 and 3,460 cm⁻¹ are associated with adsorbed water. An important feature of the modified CaO is the C–H (alkane) stretching (2,800–3,000 cm⁻¹) and bending (1,440 cm⁻¹) [13]. Bands from vibration of aromatic carbon double bonds result in increased intensity at 1,600 and 1,580 cm⁻¹ and this and the aromatic carbon–hydrogen stretch (3,060 cm⁻¹) are evidence of benzyl groups, suggesting successful modification of commercial CaO [14].

Figure 2 shows results from TG/DSC thermogravimetric analysis of commercial CaO and modified CaO. There are two steps in the TG curve in the temperature range from 400 to 700 °C because of loss of H_2O and CO_2 . Furthermore, the DSC curve of the modified CaO contained two broad peaks at 450 and 700 °C corresponding to decomposition of Ca(OH)₂ and CaCO₃ formed by hydration and



Scheme 1 The reaction between commercial CaO and benzyl bromide



Fig. 1 IR spectra of commercial CaO and modified CaO



Fig. 2 TG/DSC thermogram of modified CaO

carbonation of CaO during storage and preparation, which moves to higher temperature range compared with commercial CaO (339 and 614 $^{\circ}$ C). This indicates the thermal stability of modified CaO is enhanced.



Fig. 3 Moisture absorption by commercial CaO and modified CaO

Humidity test

A major disadvantage of CaO limiting its widespread application in a variety of reactions as a solid basic catalyst is adsorption and the poisoning by H_2O during storage and use. In this work, surface modification was investigated by anchoring an organic layer on the CaO surface to improve its stability in air. Loading with a modifier, benzyl bromide, has an important effect on moisture absorption by the catalyst during its use as a catalyst for the Henry reaction. So humidity testing of modified CaO loaded with modifier in the range 0.01-0.5 % was conducted; the results are summarized in Fig. 3. For comparison, the unloaded sample was also tested. All of the tested samples were kept in a vapor-saturated container at room temperature to enable hydration and carbonation, and the weight of each sample was measured at regular intervals. From the results it can be seen that absorption of moisture continues for all samples with time, indicating unavoidable poisoning by the atmosphere H₂O and/or CO₂. However, for the unmodified CaO particles, moisture absorption reaches to nearly 100 % within 50 h whereas only a very slight weight increase was observed for modified CaO in that time, especially for 0.2 % benzyl bromide-modified CaO, and only 5.29 % moisture absorption was observed even after 200 h. It is obvious that the surface modification can effectively improve the moisture resistance of commercial CaO.

Comparison of the activity of different catalysts

The Henry reaction can be carried out on homogeneous and heterogeneous basic catalysts, for example NaOH and Na₂CO₃, with good yield and selectivity, as shown in Scheme 2. The catalytic activity of conventional bases and commercial CaO in the Henry reaction between benzaldehyde and nitromethane was investigated under reflux conditions with 10 wt% catalyst. From the results (Fig. 4), it can be seen that yield by the catalysts is not very high under these reaction condition, and the most



Scheme 2 Henry reaction of benzaldehyde and nitromethane



Fig. 4 Performance of different catalysts in the Henry reaction of benzaldehyde and nitromethane. (amount of catalyst = 10 wt%, reaction time = 12 h, benzaldehyde-to-nitromethane = 0.05:1, reaction temperature = 102 °C)

efficient liquid base catalyst, NaOH, only yields 38.9 %. Surprisingly, CaO, a heterogeneous catalyst, had the highest activity—60.1 % yield. This can be attributes to the strongly basic sites of CaO, which are the active sites for abstraction of an α -proton from the nitromethane molecule in the initial reaction and for aiding the dehydration at the end of the reaction.

Effect of amount of catalyst

To check the effect of the amount of catalyst on reactivity, the optimum amount of catalyst was investigated for commercial CaO with a reaction time of 12 h, a benzaldehyde-to-nitromethane molar ratio of 0.05:1, and under reflux. As indicated by Table 1, for the smallest amounts of catalyst, i.e. 1 %, only 59.1 % conversion of benzaldehyde was achieved. On increasing the amount of CaO to 5 %, conversion of benzaldehyde increases to 89.2 %. The increased conversion with increasing catalyst weight can be attributed to increased availability of the catalytically active sites required for this reaction. However, when the amount of catalyst was >10 % conversion of benzaldehyde increased, which may be attributed to Michael addition between the (*E*)- β -phenyl nitroolefin and nitromethane, as suggested by Lopez et al. [15].

Table 1 Effect of amount of				
commercial CaO on Henry reaction of benzaldehyde and nitromethane	Catalyst weight ratio	Conversion of benzaldehyde (%)	Yield of (<i>E</i>)-β- phenyl nitroolefin (%)	Yield of 1-phenyl-2- nitroethanol (%)
	1	59.1	26.1	33.0
	5	89.2	29.8	59.4
Reaction time $= 12$ h.	10	94.8	82.2	12.6
benzaldehyde-to-	15	84.0	53.8	30.2
nitromethane = $0.05:1$, reaction temperature = 102 °C	20	59.2	34.9	24.3
Table 2 Effect of reactiontemperature on Henry reactionof benzaldehyde andnitromethane catalyzed by	Reaction temperature	Conversion of benzaldehyde (%)	Yield of (E)-β- phenyl nitroolefin (%)	Yield of 1-phenyl-2- nitroethanol (%)
commercial CaO	30	71.1	50.6	20.5
	40	72.1	53.3	18.8
	50	80.0	58.7	22.3
	60	88.1	57.9	30.2
	70	90.8	63.8	27.0
Reaction time $= 12$ h,	80	93.9	77.6	16.3
benzaldehyde-to-	90	96.8	80.5	16.3
nitromethane = $0.05:1$, dosage of CaO = 10 wt\%	102	93.8	83.2	10.6

Effect of reaction temperature

The effect of reaction temperature on conversion of benzaldehyde was investigated at temperatures ranging from 30 to 102 °C, using benzaldehyde-to-nitromethane molar ratio of 0.05:1 and 10 wt% CaO. Conversion of benzaldehyde to both (*E*)- β phenyl nitroolefin and 1-phenyl-2-nitroethanol increases when reaction temperature is below 60 °C, as shown in Table 2. However, conversion of benzaldehyde to its addition product, 1-phenyl-2-nitroethanol, was observed to decrease with increasing reaction temperatures above 60 °C until the temperature reached the boiling point of nitromethane, 102 °C. The reason is that 1-phenyl-2-nitroethanol tends to dehydrate, being transformed to (*E*)- β -phenyl nitroolefin at high temperatures. So the optimum reaction temperature was selected as 102 °C in subsequent experiments.

Effect of modifier loading

The loading of modifier has a substantial effect on the reactivity of modified CaO. Results for CaO catalyst modified with different amounts of benzyl bromide at a benzaldehydeto-nitromethane molar ratio of 0.05:1 under reflux are listed in Table 3. From the results it can be seen that compared with commercial CaO conversion of benzaldehyde over modified CaO is enhanced and the reaction time is greatly shortened from 12 to 5 h with highest conversion of 99.8 % when 0.001 % benzyl bromide was used for modification of the CaO. The high activity of modified CaO can be attributed to the hydrophobic layer

Table 3 Effect of modifier loading on Henry reaction of benzaldehyde and nitromethane	Modifier loading (%)	Conversion of benzaldehyde (%)	Yield of (<i>E</i>)-β- phenyl nitroolefin (%)	Yield of 1-phenyl-2- nitroethanol (%)
	1	93.7	56.8	36.9
	0.1	98.1	28.0	70.1
	0.01	98.5	15.6	82.9
	0.001	99.8	36.7	62.1
Reaction time -5 h	0.0001	97.4	33.7	63.7
benzaldehyde-to-	0.00001	96.9	52.0	44.9
nitromethane = $0.05:1$, reaction temperature = 102 °C	0.000001	96.3	60.0	36.3

formed by phenyl groups of benzyl bromide, which has the potential to improve absorption of the hydrophobic benzaldehyde and nitromethane by the CaO surface and diffusion of the compounds in the surface. There is also a very interesting change in product selectivity. Selectivity for 1-phenyl-2-nitroethanol is enhanced by use of the modified CaO catalyst, and the highest yield reaches 82.9 % for CaO catalyst modified with 0.01 % benzyl bromide; more or less modifier is of no benefit to selectivity for 1-phenyl-2-nitroethanol. Compared with the results in Table 2, the Henry reaction catalyzed by commercial CaO selectively produces (E)- β -phenyl nitroolefin, which indicates that modification reduced the basicity of CaO and resulted in reduction of deprotonation of 1-phenyl-2-nitroethanol to produce (E)- β -phenyl nitroolefin.

Catalytic performance with different benzaldehydes

The Henry reaction of nitromethane with different benzaldehydes over commercial CaO and 0.01 % benzyl bromide-modified CaO were investigated under the optimum reaction conditions (amount of catalyst = 10 wt%, reaction time = 5 h, reaction temperature = 102 °C); the results are shown in Table 4. From the results, it was found that modified CaO can catalyze the reaction giving higher yields of the dehydrated and hydrated products in a much shorter time than commercial CaO. It was, furthermore, found that substituents on the benzaldehyde substantially affect yield and the selectivity. Higher conversion is observed for benzaldehydes with electron-withdrawing groups (entries 6, 7, 8, 9) whereas electron-donor groups result in lower conversion. In reactions catalyzed by commercial CaO, irrespective of the type of benzaldehyde, selectivity for (*E*)- β -phenyl nitroolefins was higher than for 1-phenyl-2-nitroethanol. For the modified CaO, however, selectivity for (*E*)- β -phenyl nitroolefins is lower than for 1-phenyl-2-nitroethanol.

Catalytic mechanism

A possible mechanism of the Henry reaction between nitromethane (A) and benzaldehyde (B) over CaO is illustrated in Scheme 3. CaO captures a proton and promotes rearrangement of the nitromethane to form C, which is an active intermediate of the Henry reaction. Via classical nucleophilic attack of C on benzaldehyde, intermediate D is formed. In route (i), the O⁻ of D picks up an H⁺

			CaO			Modified CaO	
Entry	Benzaldehydes	Conversion of benzaldehyde (%)	Yield of (E)-β-phenyl -nitroolefin (%)	Yield of 1-phenyl-2 -nitroethanol (%)	Conversion of benzaldehyde (%)	Yield of (E)-β-phenyl -nitroolefin (%)	Yield of 1-phenyl-2 -nitroethanol (%)
1	HO	88.0	51.6	36.4	97.9	40.3	57.6
2	но осна	89.0	53.8	35.2	93.4	22.6	70.8
3	HO HO	91.2	62.1	29.1	98.9	29.4	69.5
4	H ₃ CO	74.9	45.2	29.7	80.7	31.8	48.9
5		86.6	57.7	38.9	96.3	31.3	65.0
6	O CI	92.4	80.7	12.7	87.8	10.1	77.7
7	CI	96.3	53.8	42.5	99.8	33.1	66.7
8		94.1	73.6	20.5	97.7	16.9	80.8
9	O2N NO2	97.9	56.3	41.6	99.6	20.7	78.9
10	O	86.9	74.7	12.2	87.2	8.9	78.3

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from CaO to form E; in route (ii), the Ca^{2+} picks off an O⁻ from D to form a carbocation F, and deprotonation of F results in the formation of product G.

Conclusions

In this work, an efficient catalyst for the Henry reaction of benzaldehyde and nitromethane was developed by modifying commercial CaO with an organic



Scheme 3 Possible mechanism of the Henry reaction between benzaldehyde and nitromethane over CaO

modifier. Compared with commercial CaO, the catalytic activity of the modified CaO was substantially enhanced, so the reaction time was reduced from 12 to 5 h with 99.8 % conversion of benzaldehyde under the same conditions. Selectivity for (E)- β -phenyl nitroolefins and 1-phenyl-2-nitroethanol were quite difference for CaO and modified CaO. Furthermore, the modified CaO has good stability in air, which is very important to organic reactions. Characterization by FTIR and TG showed that the modifier bonds to the surface of CaO chemically and that hydration of CaO during the modification process is very slight.

Experimental

Modification of CaO

Commercial CaO (purity 99 %) was purchased from Sigma-Aldrich. The surface modification procedure was as follows. An appropriate amount of commercial CaO particles without thermal pretreatment (2.8 g, 100–160 mesh) was added directly to a solution of benzyl bromide in methanol (40 mL) with stirring at room temperature. The amount of benzyl bromide was varied in the range from 0.01 to 0.5 %. After 24 h, the oxide was isolated, washed with methanol to remove excess modifier, and the modified CaO was obtained after vacuum drying. To increase reproducibility, the particles were sieved before use. Particles of 100–160 mesh size were selected for all experiments.

Humidity test

Commercial CaO and modified CaO particles were kept in a container under saturated humidity at room temperature for several days to enable absorption of water by the surface. The samples were weighed at regular intervals. The amount of moisture absorbed as a percentage of sample weight was evaluated by use of the following equation, where Δm is the increase in weight and m_0 is the initial weight.

$$w\% = \frac{56\Delta m}{18m_0} \times 100$$

Henry reaction activity test

The Henry reaction of benzaldehyde and nitromethane shown in Scheme 1 was conducted as follows. First, 0.5 mmol benzaldehyde (99.5 %) and 100 mmol nitromethane (99.0 %) were placed in a 50-mL round-bottomed flask equipped with a magnetic stirrer and condenser. The flask was immersed in a constant temperature bath, then approximately 0.25 mmol catalyst was introduced at room temperature. The reaction mixture was monitored by TLC. The catalyst was isolated by filtration and washed with dichloromethane (3×10 mL). The filtrate was then concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, 60–120 mesh; petroleum ether–ethyl acetate 5:1 v/v). The products were characterized by comparing ¹H NMR and mass spectrometry data with those reported in the literature.

Characterization of the catalysts

FTIR spectrophotometry (Nicolet Nexus 670, USA) was used to identify the surface group on the catalyst surface. TGA experiments were performed with Q600 SDT thermal analysis equipment (TA Instruments, USA) under a flow of air in the temperature range 25–800 °C and with a ramp rate of 10 °C min⁻¹.

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