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Effective and Green Synthesis of Methyl Pyrrole-1-carboxylate with Dimethyl Carbonate Over Solid Base

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Abstract The methyl pyrrole-1-carboxylate (1-MPC) was synthesized by highly selective one-pot *N*-methoxycarbonylation of pyrrole with dimethyl carbonate (DMC). Solid bases were found to be effective catalysts and the formation of 1-MPC was closely related to their basicity. The in-situ FTIR indicated that the role of solid base catalysts was to activate pyrrole via the formation of O–H bond and the weakening of N–H bond, which was attributed to the interaction between pyrrole and surface oxygen anion of solid base. Furthermore, the reaction temperature and the reactants molar ratio were found to be the main factors for the improvement of pyrrole conversion.

Keywords Dimethyl carbonate · Methoxycarbonylation · Solid base

1 Introduction

Methyl pyrrole-1-carboxylate (1-MPC) is an important chemical for the production of 7-azabicyclo [2.2.1]hepta-2, 5-diene, 6-Ethyl 2-methyl 2-azabicyclo[3.1.0]hex-3-ene-2, 6-dicarboxylate and new tropanes [1–3]. It was earlier synthesized from pyrrole which reacted with Grignard reagent and then converted to pyrrylmagnesium bromide, or was converted to potassium pyrrole with potassium metal in the inert solvent, and finally the esterification was performed in the presence of chloroformate [4]. In those cases, the use of Grignard reagent required the strict anhydrous condition in the reaction, and methyl chloroformate was restricted due to its toxicity. Afterwards, Jaouhari et al. reported that pyrrole was carbonylated by inserting CO_2 to form the pyrrole formic acid, and then the esterification in the alcohol solvent [5], but, noble metals or toxic reagents such as palladium and mercury salts were used as catalysts in this process. Thus, it is necessary to find a convenient and green synthetic route for the synthesis of pyrrole carboxylates.

Dimethyl carbonate (DMC), as an environmentally benign building, becomes more important in the chemical industry [7–10]. DMC was found to be an effective methoxycarbonylation reagent and used in the fields of amine [13, 14], phenol [15, 16] and ketone [17]. However, the methoxycarbonylations of heterocyclic compounds with DMC have not been reported. Here, DMC was attempted as a methoxycarbonylation reagent to the synthesis of 1-MPC from pyrrole via one-pot over solid base. In this case, no addition solvents, no expensive catalysts and no complex operations were involved in the reaction.

2 Experimental

2.1 Catalysts

The catalysts used in this investigation include calcium oxide (CaO), magnesium oxide (MgO), zirconium oxide (ZrO_2) and aluminum oxide (Al_2O_3). CaO was prepared by baking the calcium carbonate ($CaCO_3$) at 1,023 K for 4 h. MgO was got by baking the $Mg(OH)_2$ at 673 K for 4 h and ZrO_2 was obtained by baking the zirconium oxychloride ($ZrOCl_2$) at 673 K for 3 h. All catalysts were stored in the

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desiccators and were dried in the vacuumed oven for 2 h prior to use.

2.2 Characterization

The basic strength of various oxides were measured by temperature programmed desorption of adsorbed CO_2 (CO_2-TPD). Before the measurement, all samples were pretreated in Ar at 600 °C for 2 h. CO_2-TPD was carried out in a U-shaped quartz tube (i.d.6 mm) at a heating rate of 10 K/min and CO_2 desorbed from catalyst surface was detected by a Balzers Omnistar^{TM} mass spectrometer. The investigation for the interactions between CaO and reactants was performed using FTIR spectrometer of NEXUS470.

2.3 Catalytic Test

The methoxycarbonylation of pyrrole was carried out in a stainless steel autoclave equipped with a digital temperature controller. Reactants (pyrrole and DMC) and catalyst were added together to the reactor according to a definite ratio at room temperature. Then the mixture was heated to desired temperature under stirring for appropriate time. The reaction was carried out at self-generated pressure. As the reaction was finished, the reactor was cooled in ice water trap. The product samples were analyzed by gas chromatography with a HP-5 capillary column (30 m × 0.320 mm × 0.250 mm) and flamed ion detector (FID).

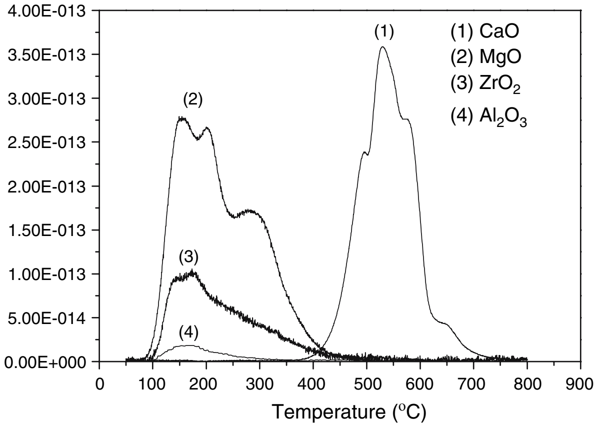


Fig. 1 The CO_2-TPD of various oxides

Table 1 Catalytic activity of various catalysts on the methoxycarbonylation of pyrrole[a]

Catalyst	CO_2 uptake (mmol/mol)	Pyrrole conversion (%)	Selectivity (%)		1-MPC yield
			1-MPC[b]	NMP[c]	
Blank	–	4.8	100	0	4.8
Al_2O_3	2.94e-3	5.6	100	0	5.6
ZrO_2	1.00	34.6	61.1	38.9	21.1
MgO	1.04	40.0	97.9	2.1	39.2
CaO	14.56	47.8	97.8	2.2	46.7

[a] Reaction condition: reaction temperature: 478 K; the molar ratio of DMC/pyrrole: 2; the molar ratio of catalyst/pyrrole: 6 mol%; the mole of pyrrole: 0.1 mol; reaction time: 3 h

[b] 1-MPC: methyl 1-pyrrole carboxylate

[c] NMP: *N*-methyl pyrrole

3 Results and Discussion

3.1 Base Properties and Catalytic Performance

Figure 1 gives the CO_2-TPD over CaO, MgO, ZrO_2 and Al_2O_3. It was found that CaO showed the strongest basic strength with the desorption at 495 °C, 530 °C, 575 °C and MgO exhibited moderate basic strength with CO_2 desorption at 150 °C, 200 °C and 290 °C, respectively. As for ZrO_2 and Al_2O_3, their desorption temperatures were observed only at 170 °C, indicating that their basic strengths were very weak. Hence, their basic strengths followed the order: CaO > MgO > $ZrO_2 \approx Al_2O_3$, and their basicity based on the CO_2 desorption amount per unit of catalyst followed the order: CaO > MgO > ZrO_2 > Al_2O_3, which was in accordance with their activity order for the synthesis of 1-MPC.

The catalytic performances of various oxides were listed in Table 1. In the absence of catalyst, only 4.8% pyrrole was converted, and Al_2O_3 was almost inactive towards pyrrole conversion. Amphoteric ZrO_2 showed the moderate catalytic performance with better pyrrole conversion and 1-MPC yield than Al_2O_3. When CaO and MgO were used as catalysts, they gave higher pyrrole conversions and 1-MPC yields than other oxides. As a result, the formation of 1-MPC was closely related to the basicity of catalyst.

3.2 Possible Catalytic Mechanism

The interaction between pyrrole and CaO was investigated by in-situ FTIR (see Fig. 2). It was found that there was no absorbance upon the surface of neat CaO at the range of 3,400–3,700 cm^{-1}. When dehydrated pyrrole was dosed to the vacuumed cell, the strong absorptions appeared at 3,518, 3,530 and 3,540 cm^{-1}, which were assigned to the stretching vibration of N–H bond (υ_{N-H}) of pyrrole. After the balance, it was interesting that the peaks at 3,518, 3,530 and 3,540 cm^{-1} decreased and a new sharp, strong peak at

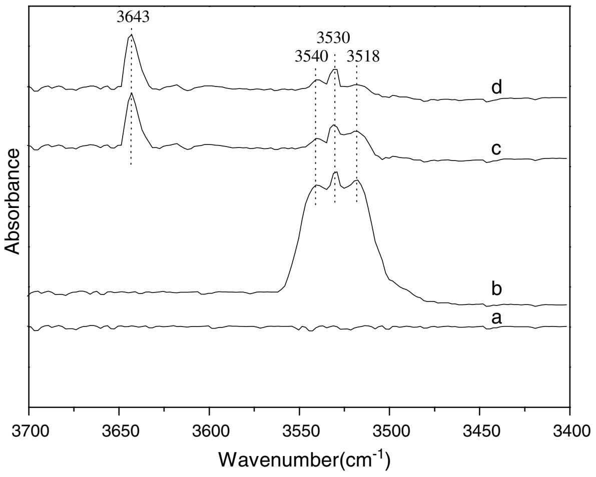


Fig. 2 IR spectra of thiophene adsorbed on CaO: (**a**) neat CaO, (**b**) after addition of pyrrole, (**c**) after balance for some time, (**d**) after removal of weakly bound molecule by vacuuming the cell

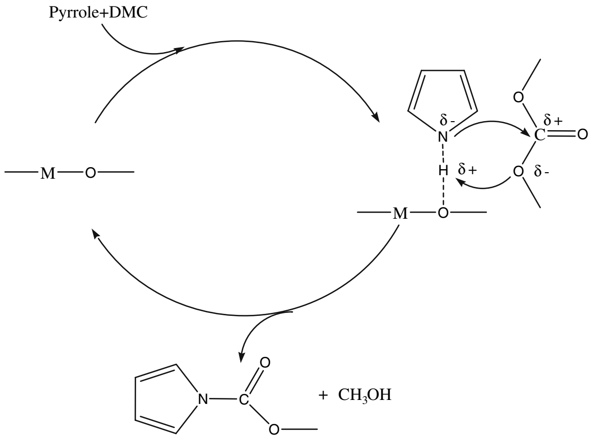
3,643 cm^{-1} appeared even if highly evacuated in vacuum. The band at 3,643 cm^{-1} was assigned to the stretching vibration of O–H bond ($\upsilon_{O\text{–}H}$) of $Ca(OH)_2$ [18]. It was reported that the peak at 3,643 cm^{-1} was formed by the reaction of CaO with atmospheric water vapor [19], while the pyrrole used in the present work was dehydrated by molecular sieve. Thus, the peak 3,643 cm^{-1} should be originated from the interaction between the surface oxygen anion of CaO and the weak acidic H atom connecting with N atom of pyrrole. In other words, pyrrole was activated by CaO via the activation of N–H bond of pyrrole. However, the interaction between CaO and DMC was not observed by in-situ FTIR. As a result, the role of base could be attributed to the activator of the N–H bond of pyrrole.

Based on the above, the possible mechanism for the formation of 1-MPC from pyrrole and DMC over basic oxides was illustrated in Scheme 1. The reaction between pyrrole and DMC over solid base might be a substitution reaction. The N–H bond of pyrrole was activated and became longer over basic oxide, and the N atom got more negative charge and attacked at the positive C atom of DMC to the formation of C–N bond. At the same time, the conjugation of O atoms of carbonate root became weaker and the C(O)–O bond longer. Those led to the broken of C(O)–O bond. As a result, 1-MPC was formed with the byproduct methanol. That was why the products were *N*-methoxycarbonylation or *N*-methylation rather than C-substitution.

3.3 Effect of Reaction Conditions

CaO was chosen as a typical catalyst to investigate the effect of reaction conditions on the methoxycarbonylation of pyrrole. It was found that the reaction temperature and the reactants molar ratio were the main factors for the improvement of the pyrrole conversion. As shown in Fig. 3, the pyrrole conversion increased with the increase of reaction temperature. The pyrrole conversion reached 5.6% at 453 K and increased to 47.8% at 478 K. With the further increased temperature, the pyrrole conversion decreased down to 43.6% at 513 K. This indicated that the deactivation of catalyst took place at high temperature, the reason of which was under investigated. However, the 1-MPC selectivity kept above 90% until the temperature increased to 493 K. At the temperature higher than 493 K, the 1-MPC selectivity decreased sharply, and the byproduct *N*-methyl pyrrole (NMP) increased rapidly. This suggested that the formation of 1-MPC and NMP was a competitive reaction.

The formation of NMP might be attributed to the decomposition of 1-MPC and the methylation of pyrrole



Scheme 1 The plausible catalytic mechanism for the formation of 1-MPC over basic oxide

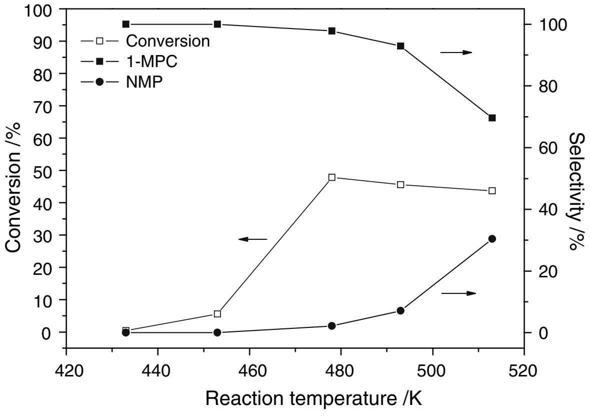


Fig. 3 The effect of reaction temperature on the pyrrole conversion and the selectivities of 1-MPC and NMP. Reaction condition: reaction time 3 h, DMC/pyrrole molar ratio 2:1, the molar ratio of catalyst/pyrrole 6 mol%

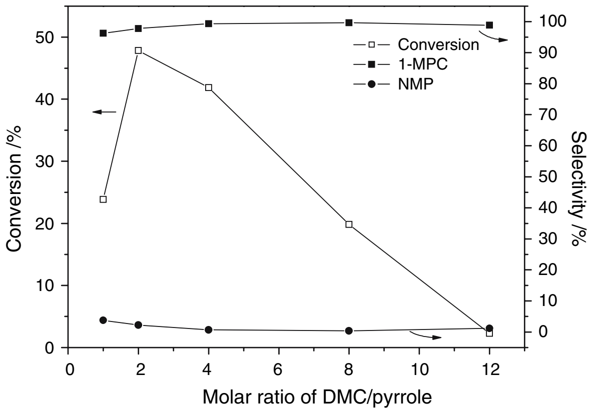


Fig. 4 The effect of molar ratio of DMC/pyrrole on the pyrrole conversion and the selectivities of 1-MPC and NMP. Reaction condition: reaction temperature 478 K, reaction time 3 h, the molar ratio of catalyst/pyrrole 6 mol%

with DMC. It was observed that 2.3% of 1-MPC decarboxylated and decomposed into NMP at 473 K. Moreover, it was reported that DMC was easy to form methyl group over oxides at high temperature [20]. Thus, high reaction temperature would be not favorable for the formation of 1-MPC.

Figure 4 shows the effect of reactant molar ratio on the methoxycarbonylation of pyrrole. With the molar ratio of DMC to pyrrole at 2, the pyrrole conversion reached highest. With the further increase of DMC, the pyrrole conversion sharply decreased, suggesting that the excessive of DMC impeded the interaction between pyrrole and catalyst. Interestingly, the selectivity of 1-MPC kept nearly 100% and hardly changed with the reactant molar ratio.

Furthermore, the conversion increased slightly with the addition of catalyst (see Fig. 5), indicating that there was strong interaction between pyrrole and basic oxides. Under the different amount of catalyst, the 1-MPC selectivity remained over 96%.

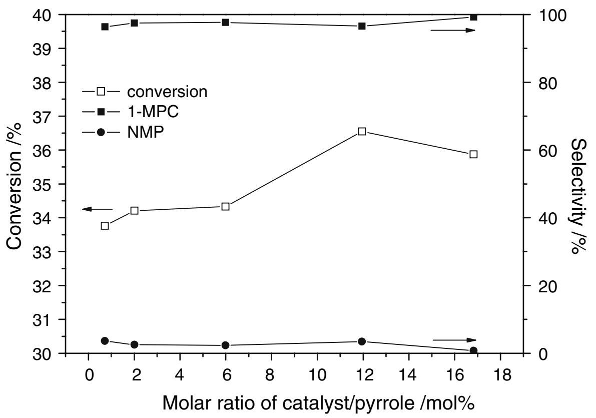


Fig. 5 The effect of molar ratio of catalyst/pyrrole on the selectivities of 1-MPC and NMP. Reaction condition: reaction temperature 478 K, reaction time 3 h, DMC/pyrrole molar ratio 2:1

4 Conclusion

The methyl pyrrole-1-carboxylate (1-MPC) was firstly one-pot synthesized with high selectivity over solid base via the direct methoxycarbonylation of pyrrole with dimethyl carbonate (DMC). The catalytic performances of various oxides were closely related to their basicity. The in-situ FTIR characterization indicated that basic oxides could activate the N-H bond of pyrrole and consequently promoted the formation of 1-MPC. All products originated from the N-substitution with exclusive regional selectivity rather than the C-substitution. In addition, the reaction temperature and the reactants molar ratio were found to be the main factors for the improvement of pyrrole conversion.

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