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Molecular shape selectivity of hydrotalcite in mixed aldol condensations of aldehydes and ketones

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Abstract

The work has engaged in the effect of activated hydrotalcite for aldol condensation of cyclic and linear ketones with *n*-heptanal and norborn-5-ene-2-carbaldehyde. A significant configuration selectivity of the catalyst was found, when the condensation of the cyclic ketones was strongly prefered in comparison with condensation of the linear ones. The mechanism of the surface reaction was predicted by the methods of molecular modeling.
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Keywords: Hydrotalcite; Aldol condensation; Molecular modeling

1. Introduction

Catalytic properties of the hydrotalcite-like compounds and related mixed oxides are intensively studied as these materials are beneficially utilized in a series of reactions – alkylation, condensation, oxidation, hydrogenation, dehydrogenation and polymerization [1–4]. One of the most progressive fields is the application of hydrotalcite-based catalysts in aldol condensation. Owing to the production of C–C bonds, these reactions have an outstanding significance in organic synthesis. However, up to now, the published studies of condensations on hydrotalcite catalysts describe mainly auto-condensation reactions of low-molecular reactive aldehydes [5,6] and acetone [7,8], mixture condensations of linear [9] or aromatic aldehydes [10,11] with acetaldehyde, acetone or acetophenone [12]. Aldol condensations on hydrotalcite of ketones, except for the two last mentioned, are not described in the literature. Activated hydrotalcites, prepared by rehydration of mixed oxides obtained by thermal decomposition of coprecipitated hydrotalcite-like precursors, yielded very good results [13]. Rehydration of rather amorphous Mg–Al mixed oxides formed during calcination of hydrotalcite was carried out in a flow of nitrogen saturated by water vapour at laboratory temperature and the layered hydrotalcite structure was restored. Contrary to the original hydrotalcite precursor prepared by coprecipitation, the rehydrated product exhibited a different morphology with lower particles and higher number of pores, edges and lattice defects [14]. Together with the property change of Lewis basic centers of oxides to the Brønsted ones of hydrotalcite, this morphology change to a more irregular arrangement has a determining significance for the catalytic activity. The exact mechanism of aldol condensation on hydrotalcite has not yet been entirely explained. The proposed models [14,15] assume that basic centers are engaged in the catalytic processes in the form of hydroxy-groups localized only at the edges of individual crystals and in their tight vicinity.

During the testing of activated hydrotalcites in aldol condensation of cyclic and linear ketones with *n*-heptanal (**1**) and norborn-5-en-2-carbaldehyde (**2**) (Scheme 1), aiming at the synthesis of fragrant substances, a significant molecular shape selectivity of the catalyst was found, strongly preferring condensation of the cyclic ketones from the linear ones. The reaction of norborn-5-en-2-carbaldehyde (**2**) with butanone (**4**) proceeded

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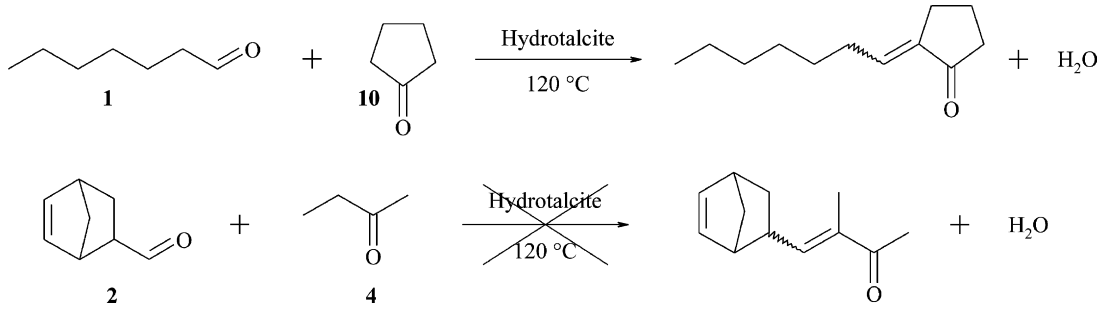

Scheme 1.

very slowly but when the same aldehyde (**2**) was condensed with cyclopentanone, the reaction rate was comparable with the condensation rate of cyclopentanone (**10**) with *n*-heptanal (**1**). These results indicated that the difference in the reactivity in case of mixed aldol condensation catalyzed by hydrotalcite is probably connected with the shape of ketone or rather with its interaction with surface of the catalyst. From the generally known mechanism of the basic-catalyzed mixed aldolization, it could be deduced that this interaction plays a key role in the production of a carbanion of ketone, which represents the initial phase of the reaction. Owing to the fact that this phenomenon as well as the condensation on hydrotalcite of the majority of the tested ketones with aldehydes are not yet described in the literature, a series of kinetic experiments was carried out to explain this phenomenon. Moreover, an effort was made to look into the mechanism of the surface reaction by using the molecular modeling.

2. Experimental

The Mg–Al hydrotalcite-like precursor was prepared by coprecipitation. An aqueous solution (450 ml) of magnesium and aluminum nitrates with Mg/Al molar ratio of 5 and total metal ion concentration of 1.0 mol l^{-1} was added dropwise to 200 ml of 0.5 M Na_2CO_3 solution under vigorous stirring. The temperature was maintained at 75 °C and pH at 10.0 ± 0.1 by a simultaneous addition of 3 M NaOH. The addition of both solutions took 1 h. The resulting suspension was then maintained at 75 °C with stirring for 1 h. The product was filtered off, washed several times with distilled water and dried at 105 °C overnight. The dried product was calcined at 550 °C for 8 h and then rehydrated for 8 h in flow of nitrogen saturated by water vapour at 25 °C. The obtained product (activated hydrotalcite) was used as catalyst in the examined condensation reactions.

Powder XRD patterns were recorded using a Seifert XRD 3000P instrument with Co Kα radiation (λ = 0.179 nm, graphite monochromator, goniometer with Bragg-Brentano geometry) in 2θ range 12–75°, step size 0.05°.

Kinetic experiments were carried out in a batch arrangement at 120 °C with the ketone to aldehyde molar ratio of 6. The quantity of hydrotalcite to 6 mmol of aldehyde was 0.1 g. The following aldehydes and ketones were used: *n*-heptanal (**1**), norborn-5-ene-2-carbaldehyde (**2**); acetone (**3**), butanone (**4**), 2-pentanone (**5**), 3-pentanone (**6**), 2-hexanone (**7**), 3-hexanone (**8**), 4-methyl-2-pentanone (**9**), cyclopentanone (**10**), cyclohexanone (**11**), cycloheptanone (**12**), 2-methylcyclopentanone (**13**), 3-methylcyclopentanone (**14**), 2-methylcyclohexanone (**15**), 4-methylcyclohexanone (**16**), 4-*tert.* butylcyclohexanone (**17**). The condensation with acetone, butanone, 2- and 3-pentanone (**3–6**), was carried out in a stirred autoclave with a heating mantle due to the boiling point of the reaction mixture.

GC analyses were performed using a HewlettPackard 5890 SERIES II Plus chromatograph equipped with FID detector and the capillary column HP-20M (50 m × 0.32 mm × 0.30 μm) with the mobile phase of N_2. The real contents of the components contained in the reaction mixtures were determined using the method of internal standard (*n*-undecane).

2.1. Description of typical experiment with substrates (3–6)

Ketone (**3–6**, 144 mmol), aldehyde (**1**,**2**, 24 mmol), *n*-undecane (1.5 g, internal standard) and a catalyst (0.4 g) sealed in a glass ampoule was introduced into a stainless steel autoclave (50 ml, Parr 5900). The autoclave was closed and heated to a reaction temperature (120 °C). The reaction was initiated by switching on the stirrer and releasing the catalyst into the reaction mixture. The frequency of the stirrer was adjusted to the value of 2200 min^{-1} assuring the kinetic course of the reaction from the point of the external mass transport, which was verified experimentally. Samples of the reaction mixture were regularly withdrawn during the course of the reaction and were analyzed using gas chromatography after their 1:50 dilution in *n*-hexane. After the reaction was terminated, the mixture in the autoclave was cooled to 20 °C and the catalyst was separated by filtration. The reaction products were further isolated.

2.2. Description of typical experiment with substrates (7–17)

The starting reaction mixture of ketone (**7–17**, 36 mmol), aldehyde (**1**,**2**, 6 mmol) and *n*-undecane (0.4 g, internal standard) was introduced to the reaction flask (10 ml) equipped with a condenser, submersed to an oil bath and under an intense stirring, heated to the reaction temperature (120 °C). The reaction was launched by adding the catalyst (0.1 g). In the course of the reaction, samples were withdrawn, which were analyzed after dilution to 1:50 by *n*-hexane using gas chromatography. In the end, the reaction mixture was cooled to 20 °C and the catalyst separated by filtration. The reaction products were not further isolated.

The mathematic models of molecules of the individual substrates were acquired by the optimization method MM+ (molecular mechanics) carried out using the software HyperChem 6.0. Based on the calculations of inter-atomic distances and the bonding angles, a concept was formed depicting the complex geometric arrangements of molecules occurring throughout the course of the catalytic reaction.

3. Results and discussion

The changes of phase composition of the coprecipitated product during calcination and rehydration procedures are demonstrated in Fig. 1. In the washed and dried product obtained by coprecipitation, a well-crystallized hydrotalcite-like phase was detected. A slight amount of hydromagnesite, $Mg_5(CO_3)_4(OH)_2{\cdot}4H_2O$, was also found in this sample as an admixture. After calcination at 550 °C, the Mg–Al mixed oxide with periclase-type structure was formed. The lattice parameter $a = 0.420$ nm of the obtained mixed oxide corresponded to the value reported for MgO (PDF 87-0653). During rehydration in wet nitrogen flow, a gradual reconstruction of the layered hydrotalcite structure can be observed. Periclase diffraction lines disappeared and only a well-crystallized hydrotalcite-like phase was detected in the samples rehydrated for 8 h and longer times.

The hydrotalcite lattice parameters a of 0.3073 and 0.3075 nm were evaluated from powder XRD patterns of the coprecipitated and completely rehydrated samples, respectively. Therefore, a rehydration of hydrotalcite-like phase formed during coprecipitation took place. A very slight and wide diffraction peak with d of about 0.48 nm was detected in the powder XRD patterns of the rehydrated samples; it can be ascribed to a slight amount of magnesium hydroxide formed during rehydration. The d_{003} basal spacing of the coprecipitated (0.79 nm) and rehydrated (0.80 nm) samples were close to each other. The carbonate and hydroxide forms of hydrotalcite exhibit only slight difference in basal spacing but the formation of hydroxide form during rehydration of calcined product in wet nitrogen flow can be expected. The phase composition of the activated hydrotalcite was not changed after its application in condensation reaction and the lattice parameters of the used catalyst remained also unchanged (Fig. 1).

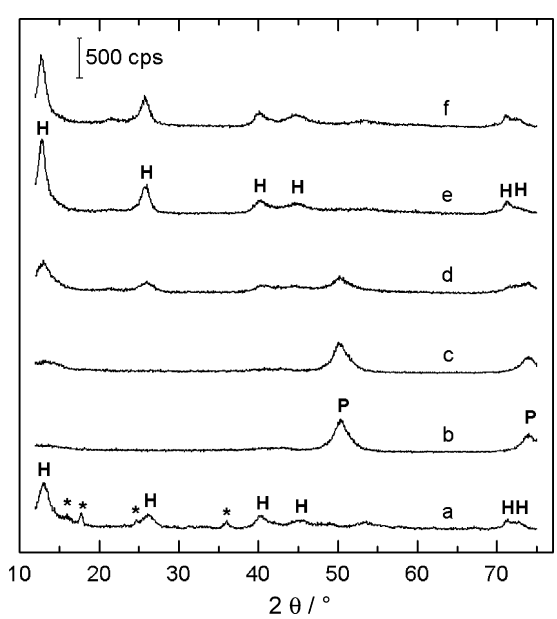

Fig. 1. Phase changes of hydrotalcite during activation: (a) coprecipitated hydrotalcite-like precursor with Mg/Al molar ratio of 5; (b) sample calcined 8 h at 550 °C; (c) calcined sample after rehydration, 1 h; (d) calcined sample after rehydration, 6 h; (e) calcined sample after rehydration, 8 h; (f) rehydrated sample (8 h) after reaction. H, hydrotalcite-like phase; P, periclase (MgO); *, hydromagnesite ($Mg_5(CO_3)_4(OH)_2{\cdot}4H_2O$).

Fig. 2a summarizes the results of the kinetic experiments, i.e. the measured initial reaction rates of aldol condensations of linear and cyclic ketones with *n*-heptanal (**1**) and norborn-5-en-2-carbaldehyde (**2**) (Scheme 1).

The measured data show that the ketone and aldehyde reactivity decreased with their increasing molecular weight. The highest difference in this respect was between acetone and other ketones. Furthermore, isomeric ketones with carbonyl group in the middle of their chain exhibited a lower reaction rate compared with alkylmethylketones at same molecular weight (3-pentanone is less reactive than 2-pentanone and the same fits to 3-hexanone and 2-hexanone).

A significant preference towards the carbanion formation in a cyclic ketone versus a linear one was observed. The reactivity of cyclohexanone was rather lower compared to cyclopentanone. The reason for the preference of cyclic ketones thus could not even be explained by the stabilization of the produced carban-

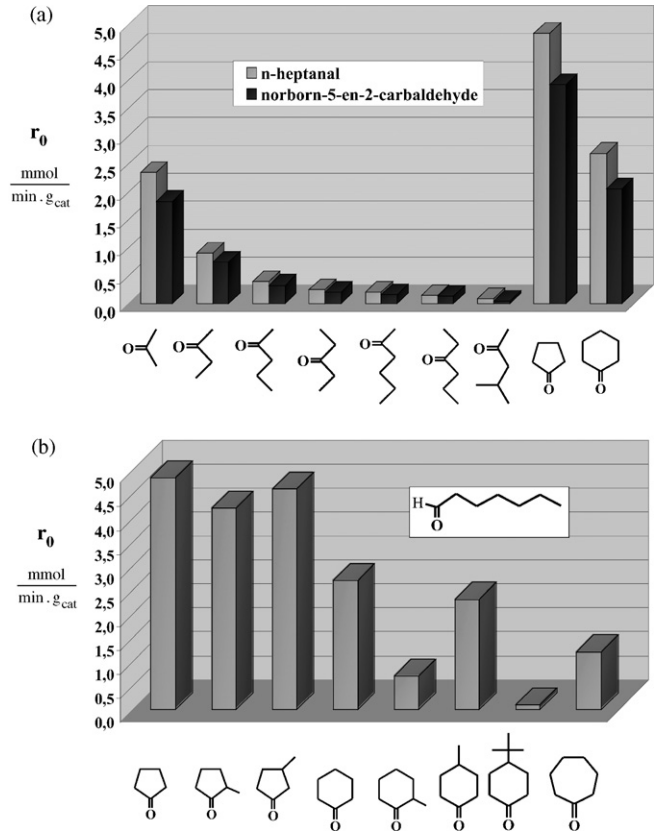

Fig. 2. Dependence of initial reaction rate of aldol condensation on ketone structure.

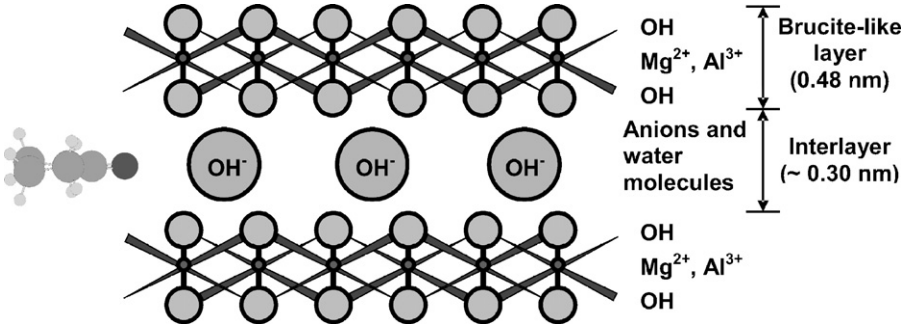

Fig. 3. Dependence of reaction rate of aldol condensation on cyclic ketone structure.

ion in the cyclic system, since β-branched ketone would have exhibited a higher stability and thus even the higher reaction rate, which to the contrary, reacted the least from all the tested substrates. The presence of a side chain complicated the carbanion production on the catalytic surface apparently owing to steric reasons. To verify this hypothesis, a further series of experiments of aldol condensations of *n*-heptanal with substituted cyclic ketones with different ring size were carried out.

Fig. 2b shows that the presence of a side chain played a negative role. This effect is the most important when the substituent is in α-position with respect to the carbonyl group and is the more important the bulkier the substituent is. *Tert*. butyl group in the position 2 was even able to prevent the reaction and in the position 4 leads to the substantially lowered reaction rate. In reference to the fact that the reaction rate observed in cycloheptanone was again significantly lower than in cyclohexanone, it could be deduced that the determining structural condition was the planarity of the entire system.

Using the software HyperChem 6.0, molecular models of the starting ketones were acquired. Having compared the calculated molecular dimensions of individual substrates with the width of hydrotalcite interlayers, it was found that these calculated data well corresponded to the measured values of the reaction rate. Taking into account the evaluated basal spacing of the activated hydrotalcite (0.80 nm) and the thickness of the brucite-like sheet (0.48 nm) [16], the interlayer width of about 0.30 nm can be considered. This dimension very well corresponded to the thickness of the molecule of nearly planar cyclopentanone, while the inter-atomic width of the most distant hydrogens was 0.24 nm (see Figs. 3 and 4). This implied that for the production of a carbanion, the intercalation of at least a part of the carbonyl skeleton to the interlayer space was necessary, where the concentration of basic centers is the highest and where the abstraction of proton from α-carbon of ketone presumably occurs, which is the first step of aldol reaction. In the very flat molecule of cyclopentanone, nothing hinders this intercalation, which corresponded to the highest measured reactivity compared to other tested ketones.

The substitution by methyl in the position 2 in cyclopentanone does not mean any extraordinary barrier compared to the case of 2-metylcyclohexanone, in which exocyclic methyl, due to having more freedom, extends above the ring level much higher than in the case of 2-metylcyclopentanone. The calculated thickness of the molecule of 0.34 nm slightly exceeded the expected width of hydrotalcite interlayers (∼0.30 nm) and it corresponded to a significantly low, rather negligible reaction rate when compared to cyclohexanone. The substitution by even larger alkyls logically created even a higher barrier. Larger and even more movable chain of cycloheptanone ranges by its dimensions at the edge of the hydrotalcite interlayers, whereas even in this case, a relatively low reaction rate was measured. Obviously, with an increasing molecular weight of a substrate in general, the reactivity decreases. Therefore, in the sequence of cyclopentanone, cyclohexanone and cycloheptanone, both of

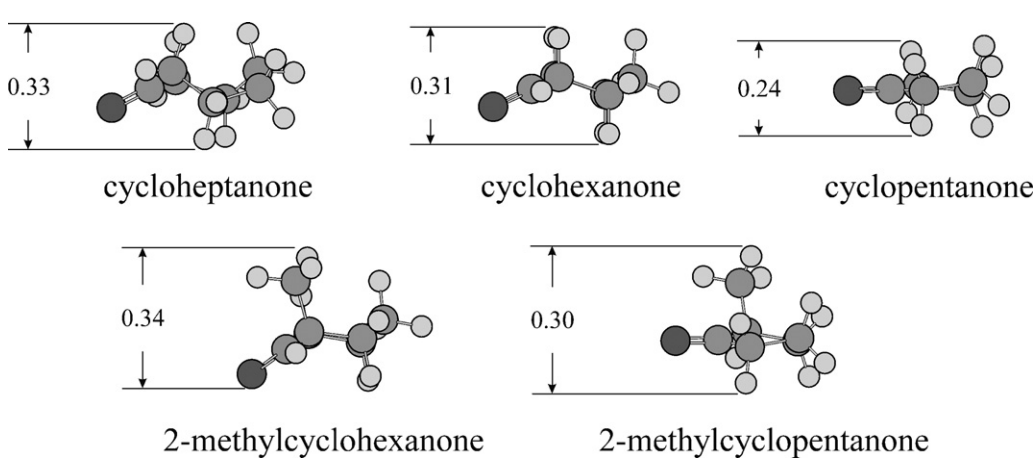

Fig. 4. Calculated thicknesses of molecules of cyclic ketones in nm.

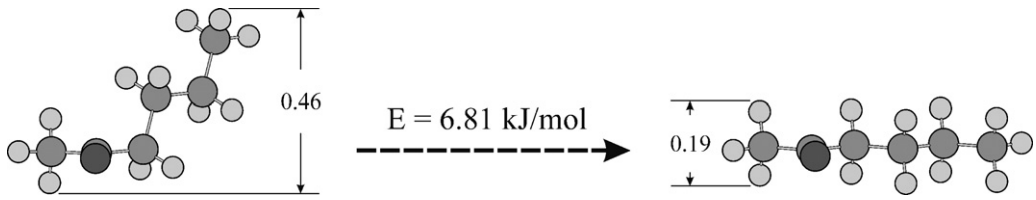

Fig. 5. Dimensions in nm of two conformers of 2-hexanone.

these effects are manifested together. Nevertheless, the effect of steric hindrance apparently plays the determinative role, which is especially apparent when comparing cyclic ketones with linear ones. It is due to an alkylic chain of linear ketones aiming askew above the level of carbonylic group, which is the thermodynamically more suitable arrangement complicating the change of conformation to a planar arrangement that would allow intercalation to hydrotalcite interlayer. The calculated value for 2-hexanone was 6.81 kJ/mol, which corresponded to the difference of relative contents of energies of individual conformers (Fig. 5). Perhaps, this also explains the fact that there is no reference in the literature describing a successful condensation of acyclic ketones besides acetone and acetophenone on hydrotalcite.

Accepting this concept about the mechanism is in concord with both of the observed essential influence of water on the catalyst activity and the concept [14] that only the centers placed on the edges of individual crystals and in their tight vicinity are involved in the catalytic processes. During the experiment with rehydrated hydrotalcite, in which the physisorbed water was separated by drying, a significant loss of activity was observed. This phenomenon is perhaps associated with dehydration, when interlayer water is released [17]. The release of water molecules from interlayers results in a decrease of the basal spacing, which can prevent an interaction between the substrate and the catalytic basic centers.

4. Conclusions

Having accomplished a series of experiments with linear and substituted cyclic ketones, a strong conformational selectivity of the catalyst versus the substrate was found. Except for acetone and to a certain degree, butanone, aldol condensation practically did not occur with acyclic ketones. The substituent next to carbonyl group in cyclic ketones significantly decreased their reactivity the more the ring of a cyclic ketone was larger and thus the further it was distant from the planar arrangement. Using the combination of the results of kinetic experiments with the ratio of dimensions of substrate molecules acquired by molecular modeling to the width of hydrotalcite interlayers, a conception was proposed about the mechanism of the surface reaction. Apparently, an intercalation of at least a part of the substrate skeleton into interlayer space is inevitable for the production of a ketone carbanion. This also to a significant degree explains the high selectivity of hydrotalcite catalysts compared to homogenous catalysts, since the consecutive activation, i.e. the production of a carbanion of a condensation product, leading to undesired consecutive reactions, is very difficult.

Acknowledgments

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