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Kinetic study of asymmetric hydrogenation of methyl levulinate using the (COD)Ru(2-methylallyl)$_2$–BINAP–HCl catalytic system

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ABSTRACT

The kinetics of asymmetric hydrogenation of methyl levulinate in the presence of the (COD)Ru(2-methylallyl)$_2$–BINAP–HCl catalytic system was studied. The kinetic order in H_2, as well as in the catalyst, was found to be equal to 1, whereas the kinetic order for the substrate and HCl falled from 1 to 0 with their increasing starting concentration. The kinetic and ^{31}P NMR data testify that the mechanism of the reaction under consideration, most likely, involves the hydride transfer to the protonated substrate in the dinuclear ruthenium complex as the rate-limiting step of the catalytic cycle.

1. Introduction

Ruthenium(II) complexes with chiral atropisomeric bisphosphine ligands, such as BINAP [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] and its analogs, are efficient catalysts for the asymmetric hydrogenation of α- and β-ketoesters [1]. At the same time, there are only a few examples of the use of γ-ketoesters in this reaction [1–8] because these compounds are considerably less active than α- and β-ketoesters. Among ruthenium-containing catalytic systems, which we tested in the asymmetric hydrogenation of ethyl levulinate used as a model γ-ketoester, the (COD)Ru(2-methylallyl)$_2$ (**1**)–BINAP–HCl system (COD–cycloocta-1,5-diene) (Ru/HCl = 5–10) was found to be most efficient [7]. In this system, the acid plays a dual role. Thus, HCl converts precatalyst **1** [9] into the dihalogenide complex followed by the substitution of COD with BINAP and serves as a promoter with respect to the in situ prepared catalyst [(BINAP)RuCl$_2$], resulting in a significant increase in the hydrogenation rate. The resulting chiral γ-hydroxy ester readily undergoes cyclization into γ-valerolactone in the course of the reaction. The hydrogenation enantioselectivity of 98–99% ee with complete conversion of γ-ketoester was achieved [7] (Scheme 1).

In the present study, the hydrogenation kinetics of methyl levulinate (**2**) in the presence of the (**1**)–BINAP–HCl catalytic system was investigated. As opposed to the transition metal-catalyzed C=C bond hydrogenation [10], the mechanism of C=O bond hydrogenation was much less well known [11–20].

2. Experimental

2.1. General

Commercial (Acros) levulinic acid, (*R*)-BINAP, and ruthenium precatalyst **1** (both from Strem) were used without additional purification. Methyl ester **2** was prepared by esterification of levulinic acid. Methanol was dehydrated and distilled under a stream of argon before use. Argon was purified by passing through columns containing a nickel/chromium catalyst, copper supported on Kieselguhr (80 °C), and molecular sieves (4 Å). Hydrogen was purified by passing through columns packed with a nickel/chromium catalyst and molecular sieves. The ^{31}P NMR spectra were recorded on a Bruker AC-200 spectrometer (81.02 MHz) with respect to 85% H_3PO_4.

2.2. General procedure for hydrogenation

A solution of ketoester **2** (500 mg, 3.8 mmol) in a mixture of MeOH (2 mL) and a 2 M solution of HCl in MeOH (95 μL, 0.19 mmol) was degassed through three freezing–evacuation–thawing–argon filling cycles. Then the degassed solution was poured into a tube for hydrogenation containing precatalyst **1** (6 mg, 0.019 mmol) and (*R*)-BINAP (12 mg, 0.019 mmol). The tube was placed in a stainless-steel autoclave (50 mL) which was purged with purified hydrogen and pressured with H_2 up to 4.3 atm. Then the reaction mixture was

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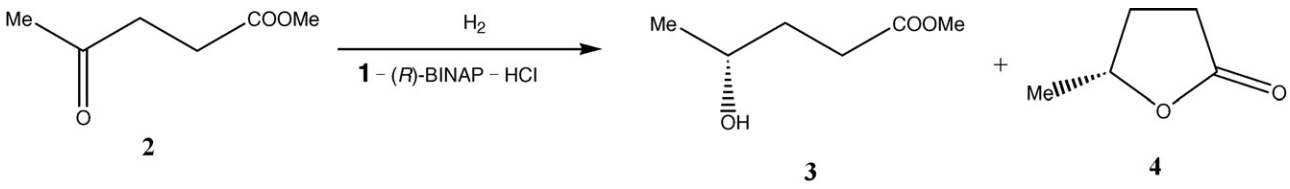


Scheme 1. Asymmetric catalytic hydrogenation of γ-ketoesters.

magnetically stirred at 60 °C. The hydrogenation experiments were carried out in the kinetic region at a stirring rate of 700 rpm. In the course of the reaction, the amount of absorbed H_2 was determined at intervals from the pressure decrease and the degree of conversion. The hydrogenation enantioselectivity determined by GLC [7] for lactone **4** was equal to 98–99% ee (*R*).

3. Results

3.1. Kinetics of hydrogenation of ketoester *2*

Fig. 1 shows that there is an induction period (20–30 min) for the hydrogenation. This can be attributed to the fact that some time is required for the formation of catalytically active particles, after which extensive hydrogenation occurs. The latter period corresponding to the 15–20% conversion of **2** is characterized by the highest hydrogenation rate (ω_{max}); and hydroxyester **3** and lactone **4** are produced in a ratio of 30/70. As can be seen from the plots in Fig. 2, the ruthenium-catalyzed hydrogenation of ketoester **2** follows first order kinetics in H_2 (a) and the catalyst (b) throughout the range of their starting concentrations. At the same time, the order in both the substrate (c) and HCl (d) changes from 1 to 0 with increasing their starting concentrations.

3.2. ^{31}P NMR study of transformations of the ruthenium catalyst

The catalyst [(BINAP)$RuCl_2$] (**A**) was prepared *in situ* by the addition of two equivalents of HCl and one equivalent of BINAP to complex **1** in acetone followed by removal of the solvent *in vacuo*. The catalyst was directly used in the hydrogenation. The ^{31}P NMR spectrum of the catalyst thus prepared (orange powder) shows two AB quartets, whose integral intensities are 1/2 (Fig. 3a). The main signals in the 29–47 ppm region of the ^{31}P NMR spectrum (a) may be assigned to a mixture of neutral dinuclear ruthenium complexes **B** and **C** (Scheme 2) containing two and three bridging chloride atoms, respectively [21–23].

After the introduction of HCl (in MeOH) into the NMR tube (HCl/Ru = 7), the red-brown solution was allowed to stand at room temperature for 2 h, and the ^{31}P NMR spectrum was again recorded. As evident from Fig. 3b, the signals in the 29–47 ppm region disappeared, and new signals at 51–59 ppm were observed. Most probably, complexes **B** and **C** interact with HCl to give an equilibrium mixture of similar anionic dinuclear complexes **D** and **E** involving bridging chloride atoms. The synthesis of this type of anionic complexes from other ruthenium precursors was documented, and these complexes were characterized by ^{31}P NMR spectroscopy [21,24,25]. As a rule, these complexes contain the quaternary tetraalkylammo-

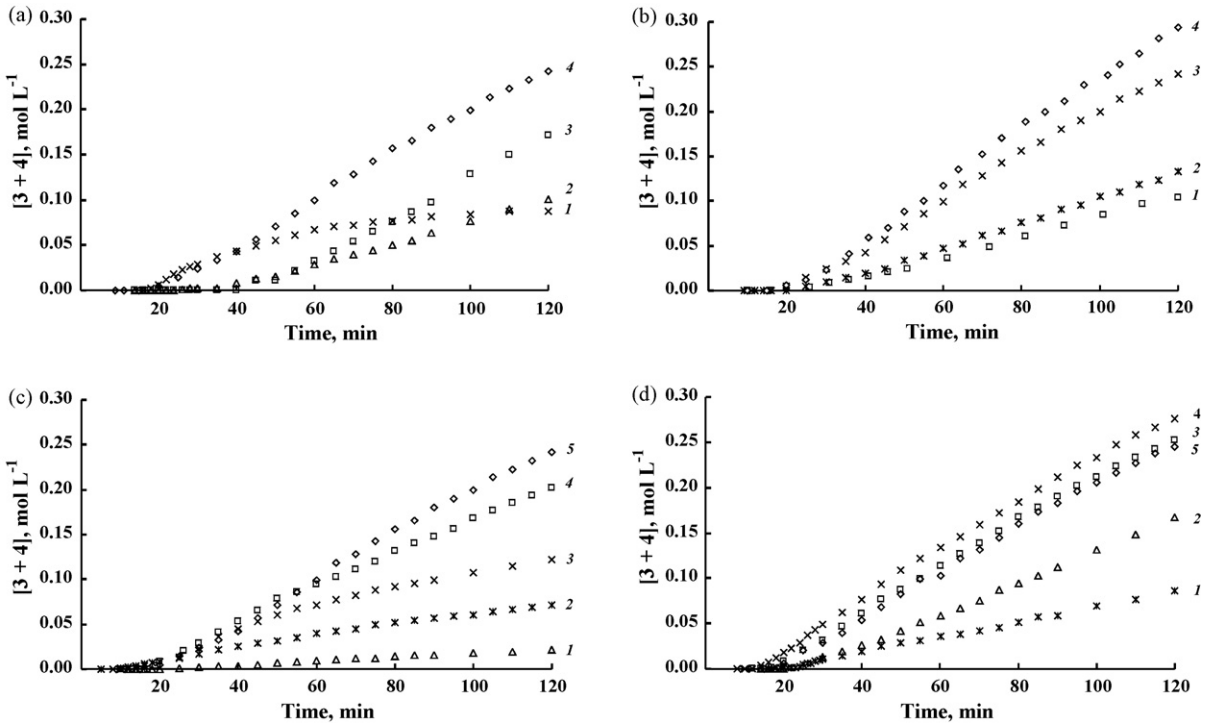


Fig. 1. Kinetics of accumulation of hydrogenation products at different starting H_2 pressures (a) and at different catalyst (b), substrate (c), and HCl (d) concentrations in anhydrous MeOH at 60 °C. Variable reaction conditions: p_0 (H_2) = 1.8 (1), 2.7 (2), 3.5 (3), 4.3 (4) atm, [Ru] = 1.41, [**2**]$_0$ = 760, [HCl] = 16.2 mmol L^{-1} (a); p_0 (H_2) = 4.3 atm, [Ru] = 0.94 (1), 1.12 (2), 1.41 (3), 1.87 (4), [**2**]$_0$ = 760, [HCl] = 16.2 mmol L^{-1} (b); p_0 (H_2) = 4.3 atm, [Ru] = 1.41, [**2**]$_0$ = 58 (1), 120 (2), 350 (3), 580 (4), 760 (5), [HCl] = 16.2 mmol L^{-1} (c); p_0 (H_2) = 4.3 atm, [Ru] = 1.41, [**2**]$_0$ = 760, [HCl] = 1.9 (1), 4.3 (2), 6.7 (3), 9.1 (4), 16.2 mmol L^{-1} (5) (d).

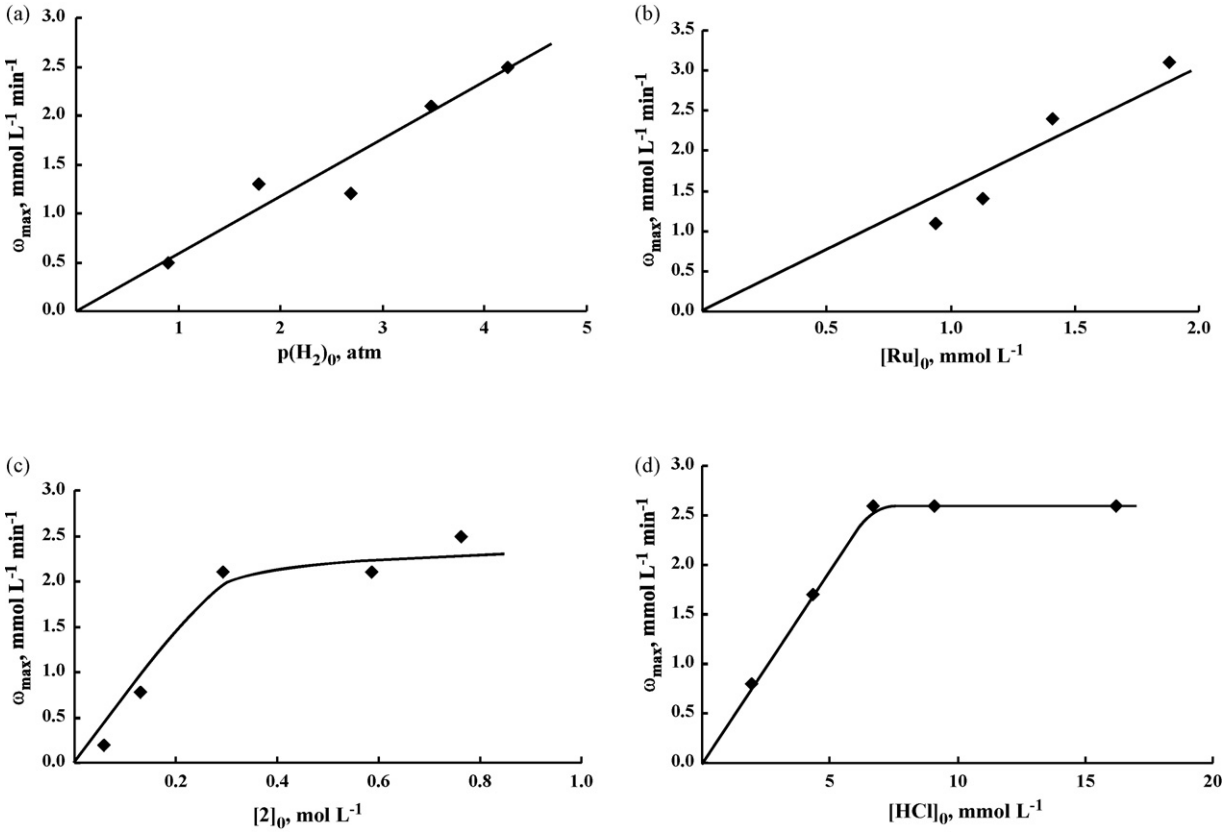


Fig. 2. Dependence of ω_{max} on the starting H_2 pressure (a) and the catalyst (b), substrate **2** (c), and HCl (d) concentrations.

nium counter-ion. To our knowledge, the only proton-containing dinuclear anionic Ru(II) complex, [{RuCl(tetra-Me-BITIOP)}$_2$(μ^2-Cl)$_3$]$^-$H$^+$ [tetra-Me-BITIOP-4,4′-bis(diphenylphosphino)-2,2′,5,5′-tetramethyl-3,3′-bithiophene], was reported until now. It was prepared by the reaction of Ru(CF$_3$COO)$_2$(tetra-Me-BITIOP) with an HCl excess. The structure of the complex was estimated by X-ray diffraction. As in the present study, the addition of HCl to the neutral ruthenium complex caused a considerable shift of the ^{31}P signals in the NMR spectrum [6].

4. Discussion

Based on the results of the present study along with the data available in the literature, the most probable mechanism of hydrogenation of γ-ketoesters in the presence of the title catalytic system can be proposed (Scheme 2).

4.1. Role of dinuclear ruthenium complexes

It is known that only the halogenide-containing ruthenium bisphosphine complexes are the active catalysts for the ketoester hydrogenation [26]. Dinuclear halogenide complexes of the **B** and **C** types have been studied in sufficient detail. In the absence of superinduced donor ligands, such as PPh_3, the equilibrium between mono- and dinuclear complexes in solution is virtually completely shifted to the latter [27,28]. In dinuclear chloride complexes, the phosphorus atoms of the bisphosphine ligand coordinated to the ruthenium atom are often spectroscopically different (the AB sys-

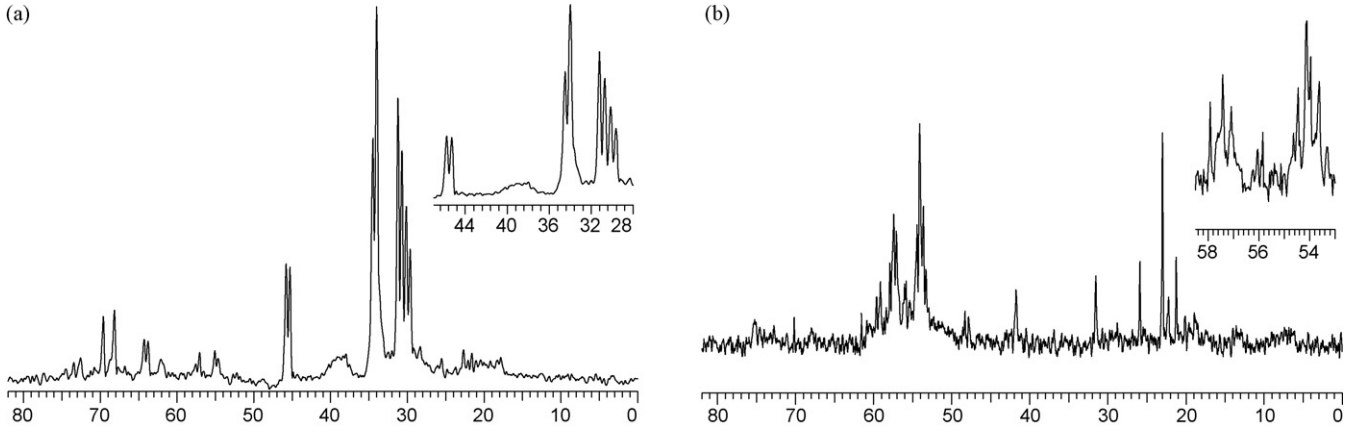
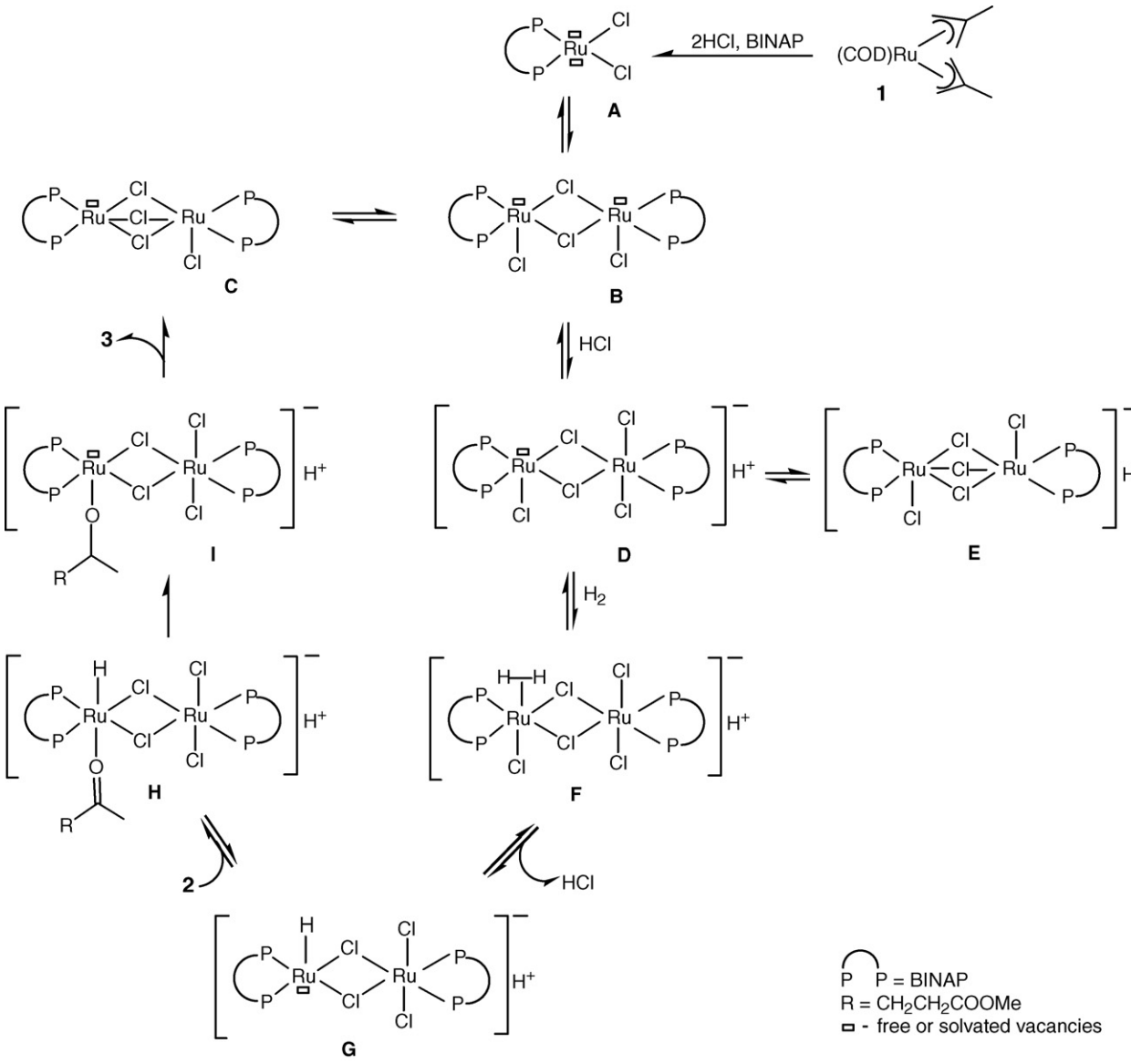


Fig. 3. The ^{31}P NMR spectrum ($CDCl_3$/MeOH = 3/1) of the catalyst prepared in situ from (COD)Ru(2-methylallyl)$_2$, (*R*)-BINAP, and HCl (1/1/2) in acetone (a), and the NMR spectrum of the same catalyst after the introduction of an acid excess ([HCl]/[Ru] = 7) into an NMR tube (b).



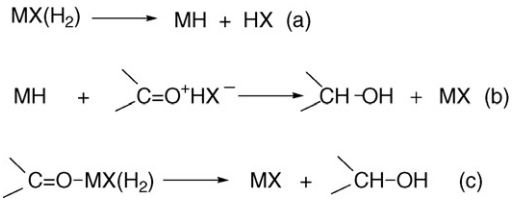
Scheme 2. Mechanism of ruthenium-catalyzed hydrogenation of γ-ketoesters.

tem in the ^{31}P NMR spectrum) even at room temperature [21]. The ^{31}P NMR spectrum assigned to dinuclear complexes **B** and **C** (Fig. 3a) is in accordance with this fact. Taking into account the results of the kinetic study (Section 3.1), non-detectable mononuclear species **A** cannot apparently be considered as catalytically active because the half order kinetics in the catalyst would be expected in the case of their reversible formation from the greatly predominant dinuclear complexes **B** or **C**. Earlier, the determining role of dinuclear complexes was found for the ruthenium-catalyzed hydrogenation of styrene [23]. Although two halogenide-containing anionic dinuclear complexes **D** and **E** would be expected to be formed by protonation of neutral intermediates **B** and **C** with HCl, only complex **D** is most likely involved in the catalytic cycle since complex **E** contains no free vacancy for the H_2 coordination.

4.2. Coordination and heterolysis of H_2

Beginning with the basic Kubas' reports [29,30], a wide range of transition metal complexes with coordinated molecular hydrogen, including ruthenium complexes [31,32], has been synthesized. Coordination of molecular hydrogen by a metal complex is ordinarily considered as the first step of catalytic hydrogenation [32]. Thus, in the course of ruthenium-catalyzed hydrogenation of 1,3-pentanedione, the dinuclear ruthenium complex of type **F** was shown (NMR) to be the main intermediate, whereas no mononuclear H_2-containing ruthenium species was detected in the reaction mixture [11]. It can be suggested that intermediate **D** having a free vacancy adds the H_2 molecule to give intermediate **F**.

Basically, the homogeneous catalytic hydrogenation of multiple bonds, including the C=O bond [32,33], may follow two alternative pathways (Scheme 3).



Scheme 3. Principal routes of the catalytic C=O bond hydrogenation through heterolysis of H_2 (a and b) and the concerted pathway (c).

Any of the pathways postulated in most publications involves heterolysis of coordinated H_2 (a) followed by hydride transfer to the protonated carbonyl group (b). Another pathway assumes the addition of coordinated H_2 to the C=O bond as a synchronous process (c). A comparative study of the kinetics of hydrogenation of ketoester **2** in MeOD and its deuteration in MeOH was carried out [20] using the **1**–BINAP–HCl catalytic system. Both processes were accompanied by rapid and reversible heterolysis of H_2 (D_2) with the involvement of the ruthenium catalyst and the protic solvent, the heterolysis rate of H_2 (D_2) being much higher than that of hydrogenation (deuteration). In addition, a kinetic isotope effect for deuteration of **2** in MeOD proved to be absent or negligible [20], whereas the k_H/k_D ratios of 2–50 were observed for ruthenium-catalyzed hydrogenation of acetophenone, which involves heterolysis of H_2 as a turnover-limiting step of the catalytic cycle [14]. The results of the present study provide evidence that the synchronous mechanism of the ruthenium-catalyzed hydrogenation (Scheme 1) is highly unlikely. Since the reaction order in the substrate changes from first to zero order with increasing starting concentration of the substrate (Fig. 2c), the coordination of **2** by ruthenium complex **F** should precede the hydrogenation step for the synchronous mechanism to be possible. However, the ruthenium ions in this complex have no vacancies to coordinate **2**. Hence, in accordance with Scheme 2, the most probable pathway for the transformation of complex **F** involves fast and reversible heterolysis of coordinated H_2 giving rise to hydride intermediate **G**.

4.3. Substrate coordination and hydride transfer

The appearance of a free vacancy at one of the ruthenium atoms in intermediate **G** as a result of heterolysis of H_2 and elimination of HCl allows the substrate to occupy this site. Based on the kinetic data obtained in the present study, the subsequent hydride transfer from the metal ion to the C=O bond in the intermediate **H** is, most likely, the rate-limiting step of catalytic hydrogenation. This step is apparently facilitated by intramolecular protonation of the coordinated ketoester. According to Scheme 2, decomposition of the intermediate anionic complex **I** gives hydroxy ester **3** and neutral complex **C** (the latter is apparently in equilibrium with complex **B**), thus providing the renewal catalytic cycle.

5. Conclusions

The mechanism of asymmetric hydrogenation of γ-ketoesters in the presence of the **1**–BINAP–HCl catalytic system, most likely, involves fast and reversible heterolysis of H_2 followed by irreversible hydride transfer to the protonated keto group of the coordinated substrate in the anionic dinuclear Ru(II) complex.

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