

Research Note

Racemization of *R*-2-amino-1-butanol over Rh-doped Co/ γ -Al₂O₃ catalyst

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Abstract

The racemization of *R*-2-amino-1-butanol proceeded effectively over a Co–Rh/ γ -Al₂O₃ catalyst in a fixed-bed reactor. The catalyst was characterized by X-ray diffraction, X-ray photoelectron spectroscopy, temperature-programmed reduction, and transmission electron microscopy. For these catalysts, Co⁰ was believed to be the active sites of the catalyst, and the presence of the optimum amount of rhodium led to highly dispersed active species. The activity, selectivity, and stability of the catalyst were demonstrated, and racemic 2-amino-1-butanol was obtained with a yield >82% under the optimum reaction conditions.

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1. Introduction

Although many efforts have been made to synthesize chiral compounds, resolution of racemic mixtures is still a common and convenient way to obtain enantiomerically pure compounds for the pharmaceutical and agricultural industries [1]. Because the theoretical yield of common resolution methods is limited to 50%, racemization of the undesirable enantiomer is necessary. Compared with the numerous detailed studies on the racemization of simple alcohols or amines [2–4], little attention has been paid to the racemization of chiral amino alcohols [5,6].

S-2-amino-1-butanol is a key intermediate for the synthesis of ethambutol hydrochloride, an important antituberculosis agent [7,8]. Typically, most processes for the synthesis of 2-amino-1-butanol produce a racemate [9–14], and enantiomerically pure *S*-2-amino-1-butanol is obtained through the resolution of racemic *R,S*-2-amino-1-butanol. The unwanted *R*-2-amino-1-butanol is converted back to the racemate for recycling. In previous studies, the racemization of *R*-2-amino-1-butanol required ammonia and could not be readily adapted to a continuous process [5,15,16].

In this paper we report a continuous process for the racemization of *R*-2-amino-1-butanol in a fixed-bed reactor. The effects of Rh in Co/ γ -Al₂O₃ catalysts were studied by X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), temperature-programmed reduction (TPR), and transmission electron microscopy (TEM) methods. The catalytic activity and stability of the Co–Rh/ γ -Al₂O₃ catalyst in the racemization of *R*-2-amino-1-butanol were also studied.

2. Experimental

2.1. Materials and catalysts

The γ -Al₂O₃ was purchased from Tianjin Research and Design Institute of Chemical Industry, Tianjin, China. *R*-2-amino-1-butanol (99%) was obtained from Xinxiang Jujing Chemical Limited Company, Xinxiang, China. Commercially available solvents and reagents were used without further purification.

The supported metal oxide catalysts were prepared by the impregnation of γ -Al₂O₃ (BET area = 165 m²/g) with an aqueous solution of the corresponding transition-metal nitrates, and then dried and calcined under air at 550 °C for 4 h. Finally, the obtained catalysts were reduced for activation in a hydrogen stream at 450 °C before use. For example, the Co_{27.2}Rh_{3.1}/ γ -Al₂O₃ catalyst was prepared as follows: 13.4 g

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Co(NO₃)₂ · 6H₂O and 3.0 g of the solution of Rh(NO₃)₂ in water (Rh content, 10.0% w/w) were dissolved in 20.0 g H₂O, then 10.0 g γ -Al₂O₃ was added to the solution. After the mixture was impregnated for 24 h, the mixture was dried at 110 °C for 10 h, calcined under nitrogen at 550 °C for 4 h, and finally reduced in a hydrogen stream at 450 °C before use. The Co and Rh content were determined by inductively coupled plasma (ICP) spectroscopy.

2.2. Catalyst characterization

The composition of the catalysts was measured with an ICP instrument. The XRD patterns of the samples were recorded with a Rigaku D/max 2500 X-ray diffractometer using Cu-K α radiation (40 kV, 100 mA) in the range 10–90°. XPS measurements were recorded with a PHI 1600 spectrometer using a Mg-K α X-ray source for excitation. A Micromeritics 2910 apparatus equipped with a TCD detector was used for TPR measurements, carried out on calcined samples at a rate of 10 °C/min using a mixture of 10% H₂/Ar. TEM was done using a TECNAT G²F-20 instrument.

2.3. Racemization procedure

The racemization of *R*-2-amino-1-butanol was carried out in a tubular fixed-bed reactor with an inner diameter of 15 mm and length of 1100 mm. The reactor was loaded with 15.0 g of catalyst. The solution of the *R*-2-amino-1-butanol in water was dosed into the reactor at a speed of 1 ml/min by a syringe pump. The temperature in the reaction zone was measured with a thermocouple located in the center of the tube and regulated by a PID cascade controller. The hydrogen pressure in the reaction system was set by a TESCOM back-pressure regulator. Finally, the reaction mixtures were collected and distilled to yield racemized 2-amino-1-butanol. The reaction mixtures were analyzed by gas chromatography—mass spectroscopy (GC-MS) using a 25-m SE-54 capillary column, and the optical rotation data were obtained with a WZZ-3 autorotation analyzer.

2.4. Data analysis

The catalyst performances were estimated by the following recovery ratio and conversion ratio:

$[\alpha]$: optical rotation conversion ratio of $[\alpha] = 100\%$, represents a racemic mixture,

conversion ratio of $[\alpha]$

$$= \left[1 - \frac{[\alpha]_D^{20} \text{ of 2-amino-1-butanol recovered by distillation}}{[\alpha]_D^{20} \text{ of 2-amino-1-butanol fed}} \right] \times 100,$$

recovery ratio of 2-amino-1-butanol

$$= \frac{\text{amount determined of 2-amino-1-butanol after the reaction}}{\text{amount fed of 2-amino-1-butanol}} \times 100.$$

Table 1

Results of different catalysts for the racemization of *R*-(–)-2-amino-1-butanol^a

Entry	Catalyst ^b	Recovery ratio (%)	Conversion ratio (%)
1	Ni _{40.2} / γ -Al ₂ O ₃	43.8	41.8
2	Cu _{39.6} / γ -Al ₂ O ₃	52.6	28.3
3	Co _{40.5} / γ -Al ₂ O ₃	78.1	100
4	Co _{29.8} / γ -Al ₂ O ₃	81.9	100
5	Co _{20.0} / γ -Al ₂ O ₃	80.3	43.7
6	Co _{27.2} Rh _{3.1} / γ -Al ₂ O ₃	89.6	100
7	Co _{27.4} Cr _{3.1} / γ -Al ₂ O ₃	88.3	98.2
8	Co _{26.8} Sr _{2.9} / γ -Al ₂ O ₃	85.9	99.2
9	Co _{27.0} Rh _{0.9} / γ -Al ₂ O ₃	87.3	100
10	Co _{27.3} Rh _{6.0} / γ -Al ₂ O ₃	83.9	97.6

^a Reaction conditions: temperature = 150 °C, hydrogen pressure = 3.0 MPa, concentration of the solution = 20%, solvent H₂O.

^b The number in this column denotes the weight percentage of each element in the final catalyst. Prepared by the common impregnation method.

3. Results and discussion

3.1. Catalyst selection and characterization

Selecting a suitable catalyst is crucial to the racemization of *R*-2-amino-1-butanol. It is well known that the nature of the racemization of a chiral amine or alcohol is the dehydrogenation/hydrogenation process in the presence of hydrogen and transition metal catalysts. In consideration of previous work [17–20], copper, nickel, and cobalt were believed to be active catalysts for this kind of reaction. Thus a series of copper-, nickel-, and cobalt-based catalysts were prepared and examined for the racemization of *R*-2-amino-1-butanol. A representative sample of the results obtained is given in Table 1.

The experimental results showed that the degree of racemization of *R*-2-amino-1-butanol was low with copper- and nickel-based catalysts, whereas the racemization proceeded effectively with cobalt-based catalysts. With the help of GC-MS, considerable amounts of the dimers of the raw materials were detected in the reaction mixtures catalyzed by copper- or nickel-based catalysts. Therefore, copper and nickel were considered to be similar or more active for the dehydrogenation of the hydroxyl group than the amino group. In contrast, the activity of cobalt for dehydrogenation is moderate; it favors the dehydrogenation of the amino group. In addition, some metals (e.g., Rh, Cr, Sr, Fe, and Mg) have been used as promoters to Co/ γ -Al₂O₃ catalysts. Subsequently, this catalyst was optimized by examining the ratios of the active components. The experimental results showed that the Co_{27.2}-Rh_{3.1}/ γ -Al₂O₃ catalyst was the most effective catalyst.

To study the effect of rhodium on the Co/ γ -Al₂O₃ catalyst, we characterized reduced Co_{29.8}/ γ -Al₂O₃ and Co_{27.2}Rh_{3.1}/ γ -Al₂O₃ samples by XRD. The XRD patterns (Fig. 1) showed the typical diffraction lines of bulk Co, accompanied by small peaks of crystalline CoAl₂O₄, which are the result of the interaction of cobalt species with the γ -Al₂O₃ carrier and its stability in the reducing atmosphere. Detection of the crystal lattice parameters proved the existence of this phase. Comparing curves a and b, the crystals of the cobalt species were found to be smaller and broader in the Co_{27.2}Rh_{3.1}/ γ -Al₂O₃ catalyst.

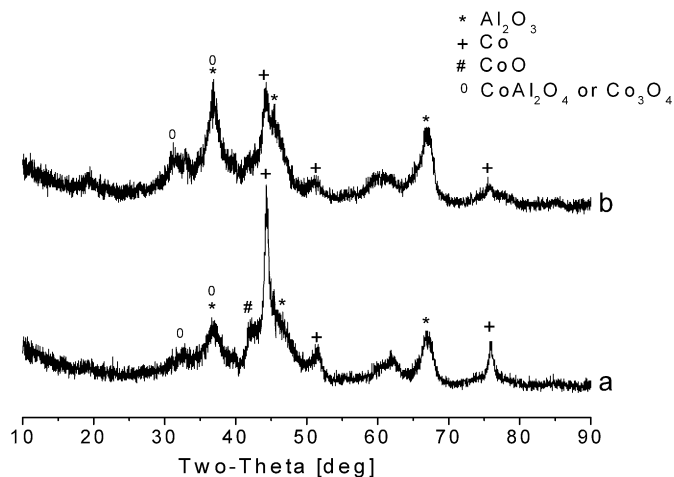


Fig. 1. XRD patterns of the $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ and $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$.

This suggests that a function of rhodium is to preserve the dispersion of the Co active species. A peak of CoO was observed in the XRD pattern of the $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ catalyst but was not found in the reduced $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalyst, implying that rhodium could improve reduction of the catalyst; however, XRD showed no indication of a rhodium phase in the sample. We suggest that Rh is present either as a highly dispersed Rh phase or as a CoRh alloy not detectable by XRD.

Fig. 2 shows the differences between the reduced $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ catalyst and the $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalyst by the XPS characterization. The binding energy of the $\text{Co}2\text{p}_{3/2}$ line is 780.5 eV in the $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ catalyst and 779.9 eV in the $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalyst. After a curve-fitting procedure was applied, Co^0 , CoO, and CoAl_2O_4 were all observed on the surface of the $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalyst. The small particle sizes and the fact that more surface Co atoms are present mean that the Co atoms are easily oxidized during the pretreatment step in the XPS measurement. This might be the reason why

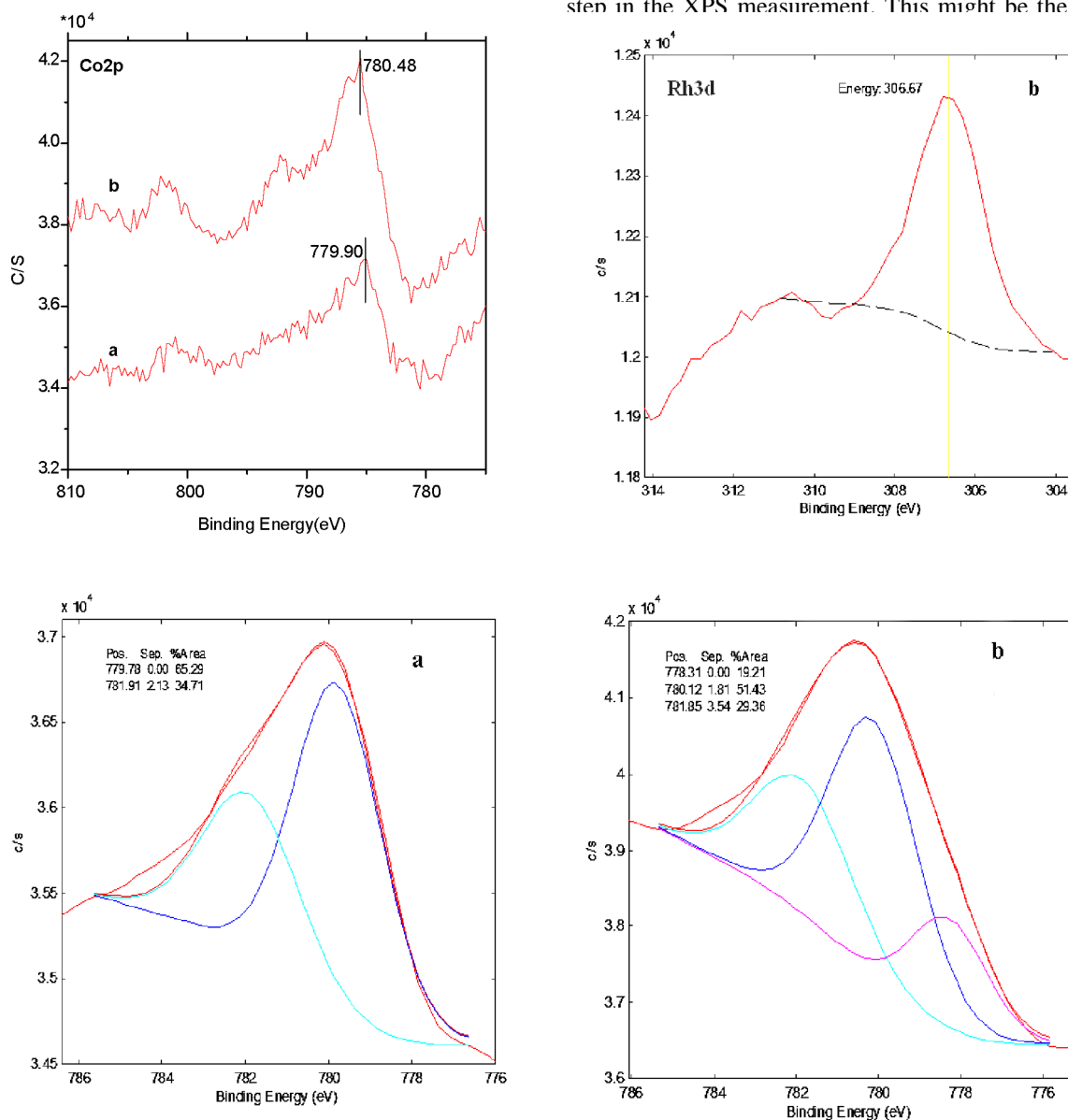


Fig. 2. XPS spectroscopy of the $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ and $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$.

Co^0 was not observed on the $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ catalyst surface. Because no racemization occurred when unreduced catalysts were used for the racemization, we conclude that Co^0 is the active center. The binding energy of Rh in the $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalyst was 306.7 eV, indicating that rhodium was present as Rh^0 , which can highly disperse the Co^0 and stabilize it. This result also supports the previous conclusion.

The TPR profile of the $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalyst showed two peaks. The main peak, at 393 °C, is due to the transformation from Co_3O_4 to CoO and is lower than that of the $\text{Co}/\gamma\text{-Al}_2\text{O}_3$ catalyst (at 407 °C); the minor peak, at 473 °C, can be ascribed to the reduction of CoO to Co and is lower than that of the $\text{Co}/\gamma\text{-Al}_2\text{O}_3$ catalyst (at 490 °C). Berge et al. pointed out that CoAl_2O_4 can be reduced only above 800–900 °C [21]; therefore, CoAl_2O_4 will not be reduced during the reduction process. The doping of rhodium was expected to affect the reduction process. These results are in agreement with the previous XRD and XPS analyses.

The surface morphologies of the $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ and $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalysts were characterized by TEM (Fig. 3). The active species particles were dispersed on the surface of the carrier, which were identified as cobalt by energy-dispersive X-ray analyses, with diameters of 10–60 and 5–30 nm, respectively. The smaller size is due to the doping of rhodium, which can be highly dispersed and can prevent sintering of the active species.

3.2. Catalytic activity testing

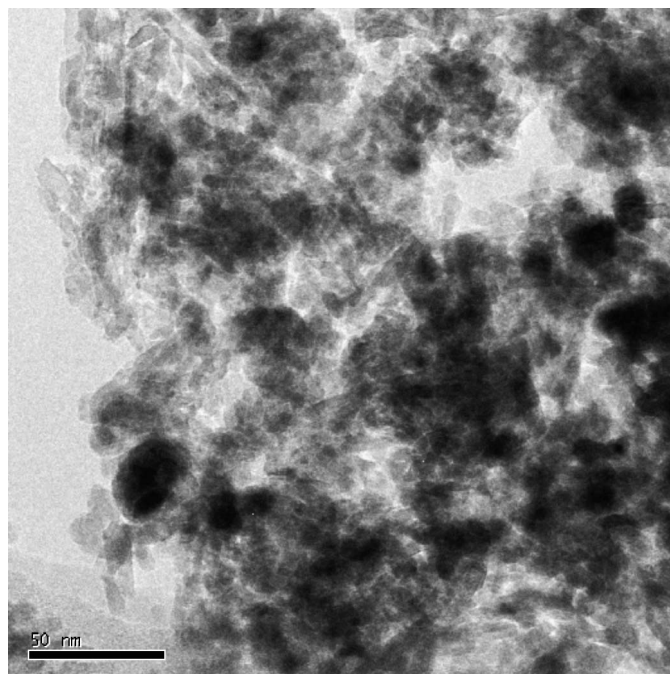
To achieve the best catalytic results, the reaction parameters, including the *R*-2-amino-1-butanol concentration of the solution, temperature, and hydrogen pressure, were optimized. Because a continuous process for the racemization of *R*-2-amino-1-butanol in a fixed-bed reactor has been proven possible, a life test had to be carried out. The life test was performed under the optimum reaction conditions over 30 days. During this period, the catalyst demonstrated excellent stability; the conversion ratio remained at 100–96.2%, and the recovery ratio remained above 86%. Thus the total yield of racemized 2-amino-1-butanol was >82%, indicating that the catalyst can be used economically in large-scale production.

4. Conclusions

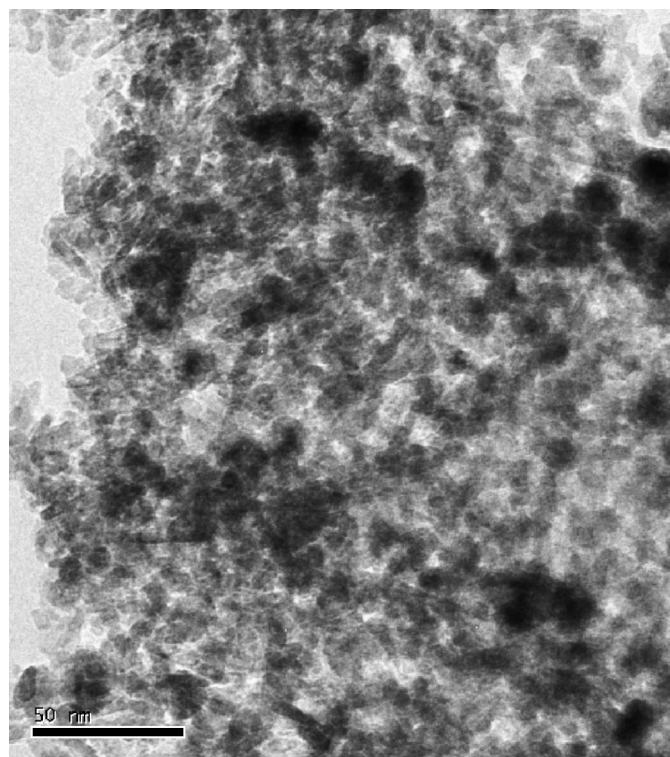
The racemization of *R*-2-amino-1-butanol over cobalt-based catalysts in a fixed-bed reactor proved to be best over a $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$ catalyst. The proper amount of rhodium led to highly dispersed active species, which can lead to more active centers and prevent the sintering of cobalt. This catalyst showed better activity and stability, and its excellent performance makes the process applicable to large-scale operations.

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(a)



(b)

Fig. 3. TEM micrographs of the $\text{Co}_{29.8}/\gamma\text{-Al}_2\text{O}_3$ and $\text{Co}_{27.2}\text{Rh}_{3.1}/\gamma\text{-Al}_2\text{O}_3$.

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