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# Enhanced catalytic performance of transition metal-doped Co/TiO<sub>2</sub> for continuous-flow synthesis of borneol from isoborneol

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Borneol, a pharmaceutically important monoterpene, has emerged as a key ingredient in modern medicinal formulations. Here, we report a highly efficient heterogeneous catalytic system using transition metal-doped Co/TiO<sub>2</sub> catalysts for the continuous-flow isomerization of isoborneol to borneol. Through systematic screening of bimetallic combinations, we demonstrate that Cu and Ni dopants synergistically enhance the redox properties of Co species, particularly improving hydrogenation–dehydrogenation efficiency in the isomerization of isoborneol. The optimized 1Cu–3Co/TiO<sub>2</sub> catalyst (Cu : Co = 1 : 3 mass ratio) enabled a two-stage continuous-flow system, achieving 58% molar yield of borneol with <0.4% camphor byproduct formation after solvent removal. Remarkably, the catalyst maintained >99% metal retention during a total of 200 h of continuous reaction. This work not only provides fundamental insights into promoter effects in bimetallic catalysis but also establishes a commercially viable platform for continuous production of high-purity botanical therapeutics.

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## 1 Introduction

Borneol (C<sub>10</sub>H<sub>18</sub>O), a bicyclic monoterpene alcohol, is a pharmacologically active compound with wide applications in both pharmaceutical and cosmetic industries.<sup>1–3</sup> Commercially available borneol exists in two distinct grades: natural and synthetic. Natural borneol, extracted from the endangered “*Dryobalanops aromatica* tree”, has limited availability and commands premium pricing, making it exclusively suitable for high-end medicinal formulations.<sup>4,5</sup> In contrast, synthetic borneol, synthesized from turpentine *via* catalytic isomerization, constitutes over 90% of the commercial market owing to its cost-effectiveness and industrial scalability.<sup>6</sup> Notably, the Chinese Pharmacopoeia (ChP) sets a minimum purity requirement of 55% for medicinal borneol, creating substantial opportunities for catalytic process innovation to improve production efficiency and product quality.<sup>7</sup>

The synthesis of borneol predominantly employs  $\alpha$ -pinene, a major turpentine derivative, as the feedstock.<sup>8</sup> However, conventional synthetic routes typically yield a low-value isoborneol as an undesired by-product.<sup>9</sup> This not only increases the cost of purification but also compromises the final product

quality.<sup>10,11</sup> Catalytic isomerization of isoborneol to borneol presents a promising strategy to both enhance the economic value of the isoborneol and upgrade the quality of borneol. Notably, the isomerization process involves competing reaction pathways, including dehydrogenation to camphor and dehydration to camphene,<sup>12</sup> as shown in Fig. 1. According to the ChP, synthetic borneol must contain less than 0.5% camphor.<sup>13</sup> Therefore, the design of highly selective bifunctional catalysts is critical to facilitate isoborneol isomerization and suppress camphor formation.<sup>14</sup>

Our previous work demonstrated a one-pot, two-step catalytic system employing NaBH<sub>4</sub>-reduced Co/TiO<sub>2</sub> catalysts, achieving 62.3% borneol yield.<sup>15,16</sup> However, this system relied on NaBH<sub>4</sub>-mediated size control of metallic Co nanoparticles, which presents scalability challenges for industrial production. Furthermore, the batch-type reaction limits large-scale borneol

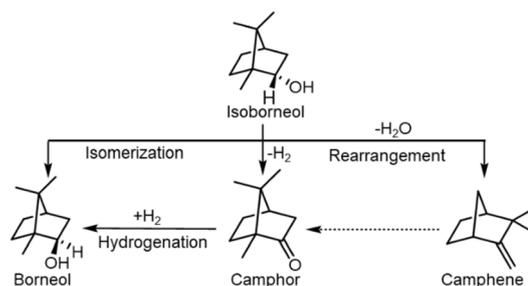


Fig. 1 Reaction mechanism of isoborneol isomerization.

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synthesis. Herein, we report a two-stage continuous-flow system using a H<sub>2</sub>-activated bimetallic M-Co/TiO<sub>2</sub> (M = Cu, Ni) catalysts to address both challenges. Transition metal doping significantly facilitates the catalysts' reduction properties while maintaining high stereoselectivity. The optimized system achieves 58% yield of borneol in continuous-flow reaction, with camphor byproduct controlled below 0.4%, which meets the requirements of the ChP.

## 2 Experimental

### 2.1 Materials

Co(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O (99%), Cu(NO<sub>3</sub>)<sub>2</sub>·3H<sub>2</sub>O (99%), Ni(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O (99%), Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (99%) and ZnCl<sub>2</sub> (99.99%) were purchased from Aladdin. TiO<sub>2</sub> (99.99%), isoborneol (97%), camphor (98%) and heptane (99%) were purchased from Adamas. All reagents were used without further purification.

### 2.2 Preparation of M-Co/TiO<sub>2</sub> catalysts

0.96 g TiO<sub>2</sub> and 0.15 g Co(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O were added to a 100 mL beaker containing 20 mL deionized water. The mixture was vigorously stirred for 3 h, then evaporated at 80 °C with stirring to dryness. The solid was vacuum-dried at 60 °C for 12 h, followed by reduction under 5 vol% H<sub>2</sub>/N<sub>2</sub> flow (10 mL min<sup>-1</sup>) by heating to 500 °C at 3 °C min<sup>-1</sup> and holding for 2 h, and then passivated under 1 vol% O<sub>2</sub>/N<sub>2</sub> flow (10 mL min<sup>-1</sup>) at room temperature for 12 h. The resulting catalyst denoted as 3Co/TiO<sub>2</sub> (3 wt% Co).

For bimetallic catalysts, 3Co/TiO<sub>2</sub> was used as the support. Specifically, 0.99 g of 3Co/TiO<sub>2</sub> and 0.04 g Cu(NO<sub>3</sub>)<sub>2</sub>·3H<sub>2</sub>O (1 wt% Cu) were dispersed in 20 mL deionized water. After stirring for 3 h, the mixture was dried and reduced under the same conditions as those used for 3Co/TiO<sub>2</sub>, the catalyst was denoted as 1Cu-3Co/TiO<sub>2</sub> (the number before each metal represents the metal's mass loading, e.g., 1 wt% Cu, 3 wt% Co). Analogously, Ni-Co/TiO<sub>2</sub>, Fe-Co/TiO<sub>2</sub>, Zn-Co/TiO<sub>2</sub> were prepared by replacing Cu(NO<sub>3</sub>)<sub>2</sub>·3H<sub>2</sub>O with Ni(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O, Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O, or ZnCl<sub>2</sub>, respectively. The 1Co-3Co/TiO<sub>2</sub> catalyst was also prepared using the same method as the bimetallic catalyst. The oxidized variant (1CuO<sub>x</sub>-3CoO<sub>x</sub>/TiO<sub>2</sub>) was obtained through calcination in air instead of H<sub>2</sub> reduction.

### 2.3 Characterizations

Powder X-ray diffraction (XRD) patterns were recorded on a Panalytical X'Pert3 diffractometer. Hydrogen temperature-programmed reduction (H<sub>2</sub>-TPR) measurements were performed using a BELCAT II chemisorption analyser. Metal loadings were determined by inductively coupled plasma mass spectrometer (ICP-MS). Transmission electron microscopy (TEM), high-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM), and energy-dispersive spectroscopy (EDS) elemental mapping measurements were performed on a JEM-F200 electron microscope. X-ray photoelectron spectroscopy (XPS) measurements were performed on a ESCALAB QXi (Thermo Scientific) using Al K $\alpha$  radiation (1846.6 eV) as the X-ray source. N<sub>2</sub> adsorption-desorption

measurements were conducted using a Micromeritics ASAP 2460 automated sorption system. More detailed characterizations are provided in SI.

### 2.4 Catalyst evaluation

**2.4.1 Isomerization of isoborneol in a batch reactor.** A 100 mL stainless steel autoclave (Shanghai LABE Instrument Co., Ltd) was charged with the catalyst (0.25 g), heptane (30 mL) and isoborneol (0.50 g). The reactor was purged five times with H<sub>2</sub> at 0.5 MPa, then pressurized to 3.0 MPa with H<sub>2</sub>. The mixture was stirred at 500 rpm while heating to 160 °C. After the reaction was complete, the reactor was cooled to room temperature.

**2.4.2 Isomerization of isoborneol in a continuous flow reactor.** The continuous isomerization of isoborneol to borneol was performed in a continuous-flow reactor (Oushisheng, H-Flow-S50), as shown in Fig. S1. The reaction tube was a stainless steel pipe (500 mm length, 20 mm inner diameter) equipped with an oil-heating jacket. Additional design and experiment are provided in the SI.

**2.4.3 Products analysis.** The reaction mixture was filtered through a 0.22  $\mu$ m syringe filter to remove the solid catalyst, and the filtrate was analyzed by gas chromatography (GC). Product identification was performed using gas chromatography-mass spectrometry (GC-MS), the corresponding spectra are provided in Fig. S2 and S3. The detailed analysis method is described in the SI. The isoborneol conversion, product yield, and Weight Hourly Space Velocity (WHSV) were calculated as follows:

$$\text{Isoborneol conversion (\%)} = (n_{\text{iso},0} - n_{\text{iso},1})/n_{\text{iso},0} \times 100\% \quad (1)$$

$$\text{Products yield (\%)} = n_i/n_{\text{iso},0} \times 100\% \quad (2)$$

$$\text{WHSV (h}^{-1}\text{)} = q_{\text{iso}}/m_c \quad (3)$$

where  $n_{\text{iso},0}$  and  $n_{\text{iso},1}$  are the molar amounts of isoborneol before and after the reaction, respectively;  $n_i$  is the molar amount of the product;  $q_{\text{iso}}$  is the mass flow rate of isoborneol;  $m_c$  is the mass of catalyst.

## 3 Results and discussions

### 3.1 The influence of the metal active sites on the isomerization of isoborneol

This work systematically investigated the catalytic performance of transition metals (Cu, Co, Ni) supported on TiO<sub>2</sub> for isoborneol isomerization, and the XRD patterns are shown in Fig. S4. As summarized in Table 1, the Co/TiO<sub>2</sub> catalyst afforded a borneol yield of >46%, whereas Cu/TiO<sub>2</sub> and Ni/TiO<sub>2</sub> yielded less than 10% under identical reaction conditions. The Cu/TiO<sub>2</sub> catalyst predominantly generated dehydrogenated products (camphor), with borneol yields below 1%. Notably, camphene formation was undetectable across all tested catalytic systems. These results suggest that Co species likely serve as the most effective active sites for isomerization of isoborneol.<sup>17-19</sup>



**Table 1** The catalytic performance of catalysts with different metal active sites<sup>a</sup>

Catalyst	Isoborneol conversion (%)	Yield (%)		
		Camphor	Camphene	Borneol
5Co/TiO <sub>2</sub>	65.45	18.67	0.00	46.41
5Cu/TiO <sub>2</sub>	13.83	13.34	0.00	0.86
5Ni/TiO <sub>2</sub>	32.35	22.86	0.00	9.83

<sup>a</sup> Reaction conditions: 0.25 g catalyst, 3 MPa H<sub>2</sub>, 160 °C, 30 mL heptane, 0.5 g isoborneol, 2 h.

### 3.2 Effect of metal loading on catalytic performance of Co/TiO<sub>2</sub> catalysts

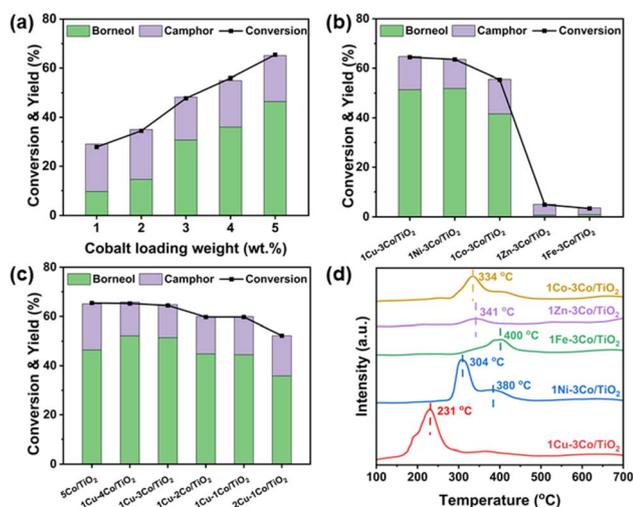
Building upon these findings, we systematically evaluated a series of Co/TiO<sub>2</sub> catalysts with varying cobalt loadings (1–5 wt%) for isoborneol isomerization, as shown in Fig. 2(a). The catalytic performance exhibited a distinct cobalt-loading dependence, with borneol yield increasing linearly from 9.7% to 46.4% as Co loading rose from 1 to 5 wt%. However, the 5 wt% Co/TiO<sub>2</sub> catalyst still generated considerable camphor byproduct (18.7%). To enhance hydrogenation activity while maintaining cost efficiency, we introduced secondary transition metals (Cu, Ni, Zn, Fe) into 3 wt% Co/TiO<sub>2</sub>, as shown in Fig. 2(b). Notably, Cu and Ni doping significantly improved the borneol yield (51.4% and 51.9%, respectively) while simultaneously suppressing camphor formation to 11.7%. In contrast, Zn and Fe incorporation caused catalyst deactivation. Further optimization of Cu–Co/TiO<sub>2</sub> revealed that increasing Co loading from 1 wt% to 3 wt% significantly improved the borneol yield, as shown in Fig. 2(c). The 1Cu–3Co/TiO<sub>2</sub> catalyst achieved a borneol yield of 51.4%, whereas 1Cu–4Co/TiO<sub>2</sub> showed a slight increase to 52.2%, with negligible change in camphor yield (<1%). Considering the balance between catalytic activity

and economic efficiency, 1Cu–3Co/TiO<sub>2</sub> was selected as the optimal catalyst.

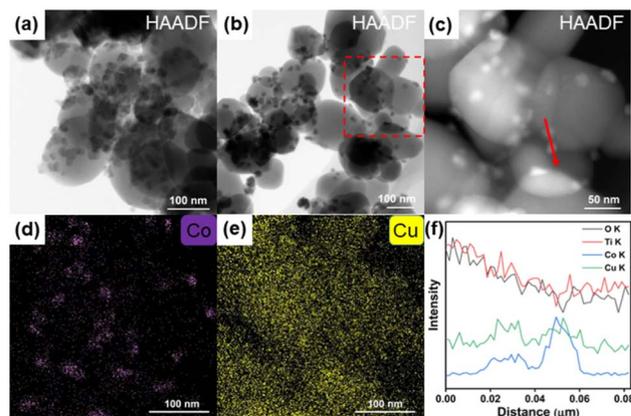
H<sub>2</sub>-TPR characterization was performed to elucidate the effect of secondary metals on the reducibility of bimetallic catalysts, as shown in Fig. 2(d). The 1Zn–3Co/TiO<sub>2</sub> catalyst displayed a prominent reduction peak at 341 °C, closely resembling that of 3Co/TiO<sub>2</sub>, suggesting that Zn incorporation exerts minimal effects on Co reducibility. In contrast, 1Fe–3Co/TiO<sub>2</sub> exhibited a broad peak shifted to ~400 °C compared to 3Co/TiO<sub>2</sub>, corresponding to the FeO → Fe<sup>0</sup> reduction process. The disappearance of the original Co peak at 334 °C suggested synergistic Co–Fe reduction at 400 °C, which increased the reduction activation energy and consequently decreased catalytic activity. The H<sub>2</sub>-TPR profile of the 1Ni–3Co/TiO<sub>2</sub> catalyst featured two distinct reduction peaks at 304 °C and 380 °C, attributed to the reduction of CoO<sub>x</sub> and NiO<sub>x</sub>, respectively. Meanwhile, the 1Cu–3Co/TiO<sub>2</sub> catalyst demonstrated a significantly lower reduction temperature at 231 °C. These results indicate that both Ni and Cu facilitate the reduction of Co, likely because their doping enhances the dispersion of Co on the TiO<sub>2</sub> support. Thereby improving the isomerization of isoborneol and hydrogenation of camphor.<sup>20–22</sup> HAADF-STEM and EDS elemental mapping showed that the 3Co/TiO<sub>2</sub> catalyst contained large and agglomerated Co particles (~14 nm), as shown in Fig. 3(a) and S5. Cu doping into 3Co/TiO<sub>2</sub> significantly reduced the Co nanoparticle size to ~12 nm, as shown in Fig. 3(b), (c) and S5. Moreover, in 1Cu–3Co/TiO<sub>2</sub>, Cu was in close contact with Co nanoparticles, and the Co distribution became more dispersed, as shown in Fig. 3(d)–(f). These results can be attributed to the high dispersibility of Cu on the support surface, which in turn enhanced the dispersion of Co on TiO<sub>2</sub>.<sup>23</sup> The Cu–Co interaction likely further improved the reducibility of the catalyst upon Cu doping (Fig. 2(d)).

### 3.3 The recyclability of the 1Cu–3Co/TiO<sub>2</sub> catalyst

The recyclability of heterogeneous catalysts is crucial for cost-effective and sustainable chemical processes. Therefore, the



**Fig. 2** The effects of metal loading for catalytic performance. (a) The influence of Co-loading weight, (b) the influence of secondary transition metals, (c) the influence of different ratio of Cu/Co, (d) H<sub>2</sub>-TPR of M-3Co/TiO<sub>2</sub> catalysts. Reaction conditions: 0.25 g catalyst, 3 MPa H<sub>2</sub>, 160 °C, 30 mL heptane, 0.5 g isoborneol, 2 h.



**Fig. 3** TEM characterizations of 3Co/TiO<sub>2</sub> and 1Cu–3Co/TiO<sub>2</sub>. (a) HAADF-STEM image of Co/TiO<sub>2</sub>. (b and c) HAADF-STEM image of 1Cu–3Co/TiO<sub>2</sub>. (d and e) EDS mapping patterns of Co and Cu over 1Cu–3Co/TiO<sub>2</sub>. (f) Line-scanning elemental distribution for 1Cu–3Co/TiO<sub>2</sub> along the red arrow in (c).



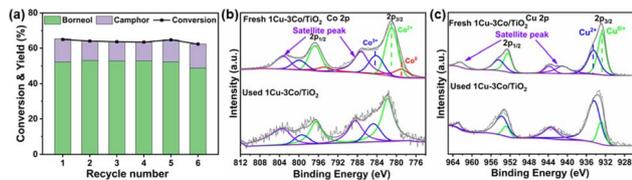


Fig. 4 The recyclability of the 1Cu-3Co/TiO<sub>2</sub> catalyst. (a) Catalytic performance, (b) Co 2p and (c) Cu 2p XPS spectra of 1Cu-3Co/TiO<sub>2</sub> before and after reaction. Reaction conditions: 0.25 g catalyst, 3 MPa H<sub>2</sub>, 160 °C, 30 mL heptane, 0.5 g isoborneol, 2 h.

stability of the bimetallic 1Cu-3Co/TiO<sub>2</sub> catalyst was evaluated in the isomerization of isoborneol to borneol, as shown in Fig. 4(a). In the recycling tests, each reaction cycle was run for 2 hours. The catalyst was then filtered, washed, and vacuum-dried for reuse. The catalyst demonstrated excellent stability during the initial five reaction cycles, maintaining a consistent borneol yield of 52.0%, while camphor formation exhibited only a marginal increase from 10.2% to 12.4%. However, a notable decline in catalytic performance occurred in the sixth cycle, with borneol yield dropping to 48.9% and camphor yield rising to 13.5%. BET analysis of 1Cu-3Co/TiO<sub>2</sub> before and after reaction revealed no significant changes in specific surface area and pore structure distribution (Fig. S6 and Table S1). In contrast, the characteristic diffraction peak at 44.3°, assigned to the (002) plane of metallic Co,<sup>24,25</sup> exhibited significant attenuation after cycling (Fig. S7), this is likely due to oxidation of metallic Co species on the catalyst surface. XPS analysis further supported this observation, and the results showed that the oxidized Co species (Co<sup>2+</sup>) increased significantly from 57.1% to 73.0% after the reaction, with the complete disappearance of Co<sup>0</sup>, as shown in Fig. 4(b) and Table S2. Combined with the observed decline in isomerization activity (Fig. 4(a)), these findings suggest that the oxidation of surface metallic Co during the reaction may deactivate the active sites, leading to reduced catalytic performance.

### 3.4 Continuous catalytic isomerization of isoborneol to borneol over a 1Cu-3Co/TiO<sub>2</sub> catalyst

While the 1Cu-3Co/TiO<sub>2</sub> catalyst exhibits high activity for the isomerization of isoborneol to borneol in a batch reactor, its practical application faces limitations due to oxidative deactivation and low production efficiency. As illustrated in Fig. S1, a two-stage continuous flow system for borneol synthesis was designed to overcome these limitations. This system not only enhances production efficiency but also prevents catalyst exposure to air, thereby enhancing long-term stability by suppressing cobalt oxidation.

The two-stage continuous-flow system first isomerizes isoborneol to yield a borneol-rich mixture containing camphor, followed by hydrogenation of camphor in the second-stage to improve product quality. Systematic parameter optimization was performed in this system for borneol synthesis. In the isomerization reaction, increasing temperature promoted both target and side reactions: borneol yield increased from 46.7% to

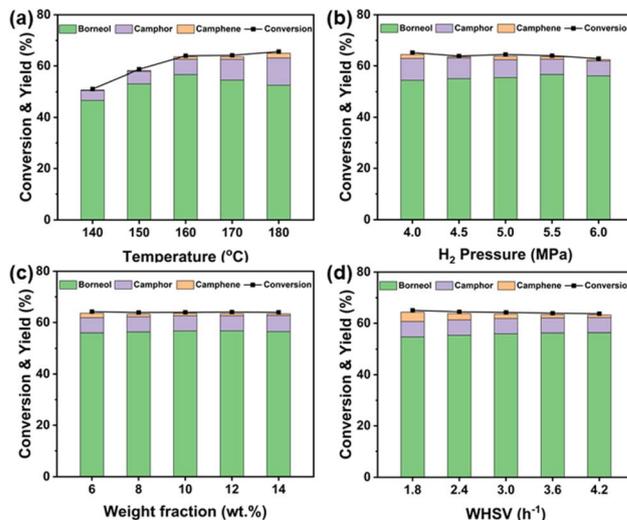


Fig. 5 The effects of reaction conditions in the isomerization stage. (a) Reaction temperatures, (b) reaction pressure, (c) substrate concentration, (d) WHSV. General reaction conditions: 160 °C, 5.5 MPa of H<sub>2</sub>, 4.2 per h WHSV, 25.5 g catalyst, and 10 wt% isoborneol.

52.6%, while camphor formation rose from 3.9% to 10.6%, as shown in Fig. 5(a). While system pressure had minimal impact on borneol yield, it significantly suppressed camphor formation (from 8.4% at 4.0 MPa to 5.7% at 6.0 MPa, Fig. 5(b)). In comparison, substrate concentration and WHSV showed slight effects on product distribution, as shown in Fig. 5(c) and (d). After comprehensive consideration of both catalytic performance and process safety, the optimal conditions were determined to be 160 °C, 5.5 MPa of H<sub>2</sub>, 4.2 per h WHSV, and 10 wt% isoborneol concentration, achieving 56.7% borneol yield with 5.9% camphor byproduct.

During the isomerization of isoborneol under optimized conditions, the borneol yield reached >55%, but the camphor content (5.9%) significantly exceeded the ChP limit of 0.5% for medicinal borneol. To comply with the standard, further hydrogenation of camphor was necessary, as shown in Fig. 6. In the hydrogenation reaction, the product mixture (composition: borneol 55.6%, camphor 5.4%, camphene 0.6%) obtained from the isomerization reaction was used as the feedstock (denoted as R<sub>0</sub>). As shown in Fig. 7(a), low temperature favored the hydrogenation of camphor to isoborneol, whereas high temperature promoted borneol formation but reduced camphor conversion. Pressure studies demonstrated that although lower pressures (4.0–4.5 MPa) maximized borneol content, the camphor content (0.57–0.62%) exceeded the ChP standards

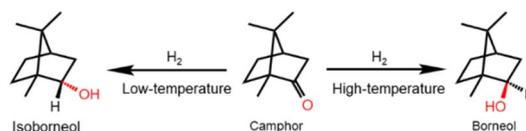


Fig. 6 Selective hydrogenation of camphor at different temperature.



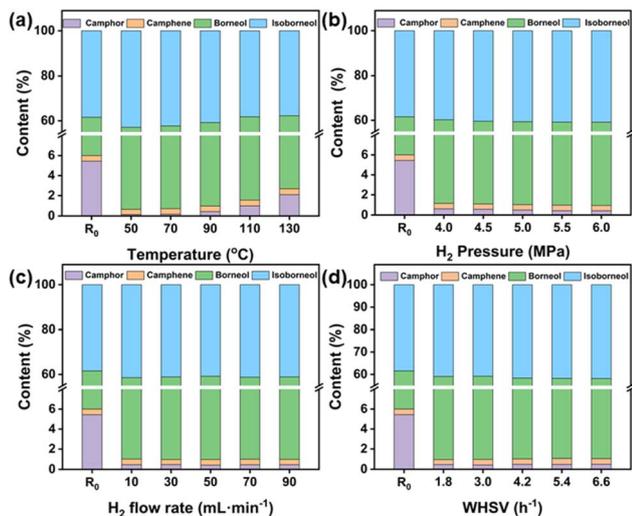


Fig. 7 The effects of reaction conditions in the hydrogenation stage. (a) Reaction temperatures, (b) reaction pressure, (c) H<sub>2</sub> flow rate, (d) WHSV. R<sub>0</sub>: the reaction products mixture from the isomerization reaction. General reaction conditions: 90 °C, 5.5 MPa of 50 mL per min H<sub>2</sub>, 3.0 per h WHSV, and 25.5 g catalyst.

(<0.5%), as shown in Fig. 7(b). At H<sub>2</sub> flow rates of 10–90 mL min<sup>-1</sup>, camphor content was effectively reduced, as shown in Fig. 7(c). At a relatively low WHSV (1.8–3.0 h<sup>-1</sup>), both borneol and camphor contents complied with ChP standards, as shown in Fig. 7(d). Based on these results, the optimal hydrogenation conditions were determined to be 90 °C, 5.5 MPa, 50 mL per min H<sub>2</sub> flow rate, and 3.0 per h WHSV.

### 3.5 The active sites for isomerization and hydrogenation

The results in Table 1 demonstrate that Co species are more effective than Cu and Ni for isoborneol isomerization. To identify whether the active site is Co<sup>0</sup> or Co<sup>2+</sup>, unreduced 1CuO<sub>x</sub>-3CoO<sub>x</sub>/TiO<sub>2</sub> was employed to catalyze the isomerization of isoborneol and the hydrogenation of camphor in a batch reactor. As summarized in Table S3, this catalyst only achieved a 23.6% borneol yield. XPS analysis revealed that 16.6% of Co<sup>0</sup> is present in the 1Cu-3Co/TiO<sub>2</sub> catalyst, whereas no Co<sup>0</sup> was detected in 1CuO<sub>x</sub>-3CoO<sub>x</sub>/TiO<sub>2</sub>, as shown in Fig. 8 and Table S2. This difference in Co<sup>0</sup> content may explain the enhanced catalytic performance of 1Cu-3Co/TiO<sub>2</sub>. Further evaluation of camphor hydrogenation revealed that 1Cu-3Co/TiO<sub>2</sub> significantly outperformed single-metal catalysts (1Cu/TiO<sub>2</sub> and 3Co/

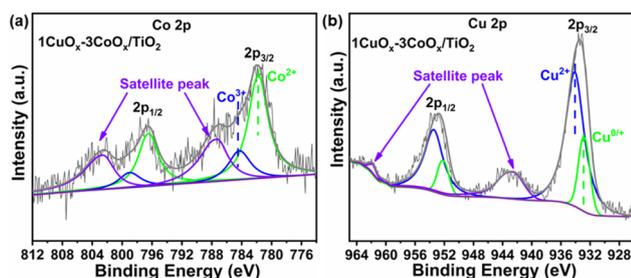


Fig. 8 XPS spectra of 1CuO<sub>x</sub>-3CoO<sub>x</sub>/TiO<sub>2</sub>. (a) Cu 2p, (b) Co 2p.

TiO<sub>2</sub>) and the unreduced 1CuO<sub>x</sub>-3CoO<sub>x</sub>/TiO<sub>2</sub> catalyst. Notably, the 3Co/TiO<sub>2</sub> exhibited weak activity, whereas the 1Cu/TiO<sub>2</sub> and 1CuO<sub>x</sub>-3CoO<sub>x</sub>/TiO<sub>2</sub> were inactive under the tested conditions (Table S3). These results indicate that both Co<sup>0</sup> and Co<sup>2+</sup> can catalyze the isomerization of isoborneol. However, Co<sup>0</sup> exhibits significantly higher catalytic activity than Co<sup>2+</sup>, establishing it as the predominant active site. Furthermore, the hydrogenation of camphor occurs exclusively on the surface of Co<sup>0</sup>. Cu doping enhances the dispersion of Co on TiO<sub>2</sub>, thereby improving catalytic efficiency in both reactions (Fig. 3).

### 3.6 The long-term stability of the 1Cu-3Co/TiO<sub>2</sub> in the two-stage continuous flow reactor

Building upon the optimized reaction conditions established for high-temperature isomerization (160 °C, 5.5 MPa) and low-temperature hydrogenation (90 °C, 5.5 MPa), we systematically evaluated the long-term stability of the 1Cu-3Co/TiO<sub>2</sub> catalyst in isomerization and hydrogenation reactions, as shown in Fig. 9. The catalyst exhibited exceptional performance during 100 h continuous isomerization, maintaining stable borneol yields exceeding 55.0% while effectively controlling camphor formation at 5.5%. Subsequent direct utilization of the isomerization products in the hydrogenation stage revealed remarkable catalytic durability, with borneol content showing only a minimal decrease from 58.3% to 56.8% over 100 h of reaction, while camphor content remained <0.5%. This integrated process successfully synthesized high-quality borneol, with borneol content >57% and camphor content below 0.5%, fully complying with the ChP standards. ICP-MS analysis revealed minimal metal leaching (Co loss: 1.75 wt%; Cu loss:

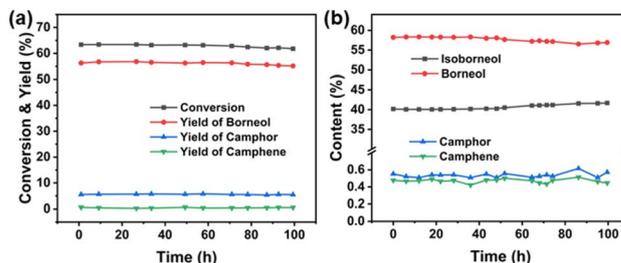


Fig. 9 Stability test of 1Cu-3Co/TiO<sub>2</sub> in the two stage reaction. (a) Isomerization stage, (b) hydrogenation stage. Reaction conditions: 5.5 MPa of 50 mL per min H<sub>2</sub>, 25.5 g catalyst, and 10 wt% isoborneol, 160 °C, 3.0 per h WHSV for isomerization and 90 °C, 2.4 per h WHSV for hydrogenation (To avoid pipeline blockage from borneol precipitation in heptane under low-temperature conditions, the WHSV was maintained at 2.4 h<sup>-1</sup>).

Table 2 Loadings of Co and Cu in the 1Cu-3Co/TiO<sub>2</sub> bimetallic catalyst before and after reaction

Catalyst	Elemental content (wt%)	
	Co	Cu
Fresh 1Cu-3Co/TiO <sub>2</sub>	3.0737	1.0595
Used 1Cu-3Co/TiO <sub>2</sub>	3.0199	1.0083



Table 3 Composition analysis of products before and after purification<sup>a</sup>

Sample	Content (%)				
	<i>n</i> -Hep.	CPE	CPO	Isobor.	Bor.
Crude product	—	0.52	0.48	40.59	57.09
Purified product	0.52	0.15	0.35	39.93	57.94
Solvent	99.80	0.03	0.005	0.09	0.07

<sup>a</sup> *n*-Hep.: *n*-heptane; CPE: camphene; CPO: camphor; isobor.: isoborneol; bor.: borneol.

Table 4 Residual Co and Cu content in solvents and products after purification

Sample	Elemental content (ppm)	
	Co	Cu
Recovered solvent	100	100
Purified product	200	<100

4.83 wt%, relative to initial loading, Table 2) after 200 h of total reaction, confirming outstanding structural stability.

### 3.7 The purification of the crude borneol products

The crude borneol products were purified through vacuum rotary evaporation (40 °C, 2 kPa) to remove residual solvents, followed by gas chromatographic (GC) analysis to determine the purity of both the recovered solvents and crystalline products. As summarized in Table 3, the final product exhibited high purity, with a composition of 57.9% borneol and 0.35% camphor, fully meeting the purity requirements of the ChP. Notably, ICP-MS analysis detected minimal metal leaching in both the recovered solvents (Co < 100 ppm, Cu < 100 ppm) and purified borneol product (Co < 200 ppm, Cu < 100 ppm), as shown in Table 4. These results demonstrate not only the exceptional stability of the 1Cu–3Co/TiO<sub>2</sub> catalyst under prolonged reaction conditions but also the absence of significant metal contamination in the product, suggesting its potential for high-quality borneol synthesis.

## 4 Conclusions

This work demonstrates an efficient continuous process for high-quality borneol production through tandem high- and low-temperature catalytic stages. Using a bimetallic 1Cu–3Co/TiO<sub>2</sub> catalyst in a two-stage continuous-flow system, the final product (after solvent removal) contained 58.0% borneol with <0.4% camphor, fully complying with ChP standards. The research revealed that Cu and Ni dopants significantly facilitated the reduction of surface Co species, thereby enhancing catalytic activity. In contrast, Fe and Zn dopants formed surface layers that physically blocked Co active sites and reduced performance. Under optimized conditions, the 1Cu–3Co/TiO<sub>2</sub> catalyst maintained stable activity for at least 200 h, demonstrating its

potential for continuous isoborneol upgrading in industrial applications.

## Author contributions

This manuscript was written with contributions from all authors. Chenyang Li and Zhihan Liu: data curation, formal analysis, investigation, and writing – original draft. Huimin Li, Yuanseng Xiao, Ying Huang and Yuting Liu: data curation. Jie Liu and Bin Wu: visualization. Fuweng Zhang: writing – review & editing. Huidong Zheng: resources and project administration. Longfei Yan: conceptualization, funding acquisition, methodology and writing – review & editing.

## Conflicts of interest

There are no conflicts to declare.

## Data availability

All data generated or analyzed during this study are included in this manuscript and the SI. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. Data are openly available in a public repository.

Additional details supporting the findings of this study are available in the SI. See DOI: <https://doi.org/10.1039/d5ra03723a>.

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