

An Experimental Modification to the Preparation of di-*n*-butyl ether from 1-butanol for the Undergraduate Teaching Course of Organic Laboratory

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Abstract To explore a greener and safer experimental preparation method for di-*n*-butyl ether, a modification to the preparation of di-*n*-butyl ether from 1-butanol was used in this study by replacing the traditional concentrated sulfuric acid as the catalyst with *p*-toluenesulfonic acid under the guidance of computational calculations. The effects of reaction temperature, catalyst quantity, and other parameters on the reaction were investigated. The catalyst's recovery and reuse were explored. The results reveal that *p*-toluenesulfonic acid has a catalytic efficiency comparable to that of concentrated sulfuric acid in this experiment, that it is safer and easier to operate, and that it can be recovered and reused using simple procedures, which meets the requirements of green chemistry. The findings of this study may be utilized to enhance the di-*n*-butyl ether preparation experiment, which can be used in the Organic Chemistry Laboratory course at colleges.

Keywords: experimental modification, preparation, di-*n*-dibutyl ether, *p*-toluenesulfonic acid, green chemistry

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The preparation of di-*n*-butyl ether is a fundamental experiment in the Organic Chemistry Laboratory course at college. Most published Organic Chemistry Laboratory textbooks describe the preparation of di-*n*-butyl ether from 1-butanol catalyzed by concentrated sulfuric acid in a setup equipped with a Dean-Stark trap to capture the water generated during the reaction process and promote the forward reaction [1]. Because about 27% (mol) rather than a catalytic amount of concentrated sulfuric acid is used in this experiment, the risk factor of the reaction is greatly increased due to the strong corrosiveness of concentrated sulfuric acid, and the complexity of the reaction is greatly increased due to the catalyst's strong oxidizing and dehydrating properties. Furthermore, the production of a large amount of waste acid does not comply with green chemistry guidelines. As a result, in this experiment, improvements in catalyst replacement and reaction condition control are highly required.

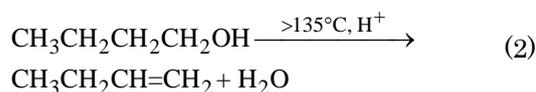
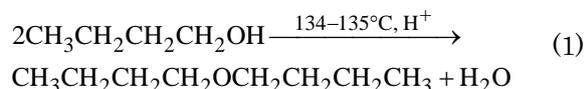
Some attempts have been made in recent years to modify this experiment and make it more acceptable for use in the Organic Chemistry Laboratory. For example, Qin et al. advised lowering the quantity of concentrated sulfuric acid and raising the reaction's ultimate temperature to reduce waste acid generation while maintaining a satisfactory yield [2]; Dou et al. proposed directly employing the Dean-stark trap as a distillation collector, therefore increasing the experiment's efficiency

[3]. However, in this experiment, little consideration has been paid to replacing concentrated sulfuric acid with different catalysts. This suggests the need for a recyclable and safer catalyst, allowing for the safe, ecologically friendly, and efficient production of di-*n*-butyl ether.

In our previous work, an in-depth analysis was conducted on the mechanism of this reaction by using computational chemistry tools [4]. The reaction mechanism was investigated, which included the reaction routes, transition states, energy changes, and rate constants of the main and side reactions in the reaction system. The data demonstrate that there are primarily two reaction routes in this reaction system, with the one from 1-butanol to di-*n*-butyl ether (ether-forming) being the main reaction and the one from 1-butene to 1-butene (olefin-forming) being the side reaction. However, when the reaction temperature is below 380 K, both the ether-forming and olefin-forming reactions are very slow; when the reaction temperature exceeds 400 K, both reaction paths are significantly accelerated, and the olefin-forming reaction becomes very obvious when the reacting mixture is heated up to 420 K. As a result, the reaction temperature must be higher than 380 K to guarantee that the intended main reaction occurs smoothly and at an acceptable rate, and lower than 420 K to avoid excessive elimination product production. As a consequence, maintaining a temperature range of 130 to 140°C is critical in the reaction system. It

is discovered that if no additional high boiling point solvents are added to the reaction system, the temperature of the reaction system is extremely difficult to reach 130°C, and the excessive sulfuric acid acts not only as a catalyst but also as a high boiling point solvent to enhance the boiling point of the reaction mixture solution so that a sufficient reaction temperature can be attained in a short period.

The catalytic effects of some solid acids, including Amberlyst-15, NaHSO₄·H₂O, NaHSO₃, and some others, were investigated based on computational chemistry findings. The results demonstrated that, even though all of these catalysts are strong acids, they are unable to successfully accelerate the process. After 4 hours of refluxing in the presence of 25% (mol) of either of these solid acids, the temperature of the reaction mixture solution remains about 118°C, and there is no visible change in the water surface in the Dean-Stark trap, indicating that the reaction scarcely happens. This confirmed the prior theoretical investigation's findings, demonstrating that the reaction is exceedingly slow at temperatures below 130°C. If a speedy reaction is desired, the temperature of the reaction system must be quickly raised to 130°C, which requires raising the boiling point of the reaction mixture solution. Based on this analysis, it is hypothesized that *p*-toluenesulfonic acid, a low-melting, and safer acid, can replace sulfuric acid in this process by providing both a strong acid and a high boiling point. As a result, the use of *p*-toluenesulfonic acid in this reaction system is investigated in this work.



1. Experimental Part

1.1. Principle

The main and side reactions in this reaction system are the ether-forming and olefin-forming, respectively. The reaction equations are shown in Equations 1 and 2 respectively [1]. Because 1-butanol is a primary alcohol, the ether-forming substitution reaction, and the olefin-forming elimination reaction follow the S_N2 and E2 mechanisms, respectively. The attacking reagents attack the α-C and β-H of the protonated 1-butanol, generating di-*n*-butyl ether as the major product and 1-butene as a by-product. The ether-forming substitution process and the olefin-forming elimination reaction are competing for reactions in this reaction system, and the temperature necessary for the elimination reaction is often higher than that required for the substitution reaction. As a consequence, to ensure that the ether-forming process may occur quickly at a high temperature; simultaneously, to avoid the side reaction of olefin production when the temperature is too high, the reaction temperature must be tightly controlled.

1.2. Experimental Process

To a reflux device with a Dean-stark trap, 15.5 mL of 1-butanol was added to the 100 mL two-necked round bottom flask, a specified amount of catalyst was applied, and (V-2) mL of water was introduced to the Dean-Stark trap. The reaction mixture was gradually heated until the solution boiled, and then the reflux was maintained at a speed that kept the reflux liquids dropping at a rate of 2-3 drops per second for 0.5 hours. After 3 hours of refluxing, the reflux equipment was replaced with a standard distillation apparatus to collect the fraction at 115-122°C. The remaining liquid in the flask was poured into a beaker while it was still hot and cooled. The obtained solid was washed twice with 10 mL of petroleum ether each time and drained to produce the recovered catalyst. The distillate was dried with calcium oxide, and the yield of di-*n*-butyl ether was determined using gas chromatography.

The reference experiment was carried out using concentrated sulfuric acid as the catalyst, as described in the textbook [5].

2. Results and Discussion

2.1. Experimental Phenomena

In this system, the temperature rises fast, accelerating the water separation process. Ordinary distillation is used to recover the *p*-toluenesulfonic acid solid. Meanwhile, when the temperature exceeds 127°C, the water level in the Dean-Stark trap begins to increase significantly. This occurrence may imply that as the temperature climbs to 127°C, the reaction rate accelerates markedly. When the temperature rises to 132°C, the water level in the water trap rises steadily and approaches the branch outlet, suggesting that the ether formation process has moved closer to the reversible reaction's equilibrium point.

Analysis reveals that *p*-toluenesulfonic acid has a good catalytic activity; nevertheless, its monohydrate is well soluble in 1-butanol, providing a homogenous reaction system with a higher boiling point, allowing the reaction to be completed in teaching-scheduled time with a good yield.

2.2. The Influence of Reaction Conditions on the Yield under the Catalysis of *p*-toluenesulfonic Acid

2.2.1. The Influence of the Catalyst Dosage on the Yield

The results in Table 1 demonstrate that when the amount of catalyst is sufficient, the reaction time is relatively short; however, if the temperature of the system is too high, side reactions rise and the yield drops drastically. Better yields can be obtained with different quantities of catalyst when the reaction time is long enough, but when the quantity of catalyst is minimal, an excessively lengthy reaction time is necessary. When the catalyst concentration is 22.0 percent (mole fraction), the yield is 44.8 percent with a reaction time of 213 minutes,

indicating that the catalyst quantity is reasonable, the catalytic effect is good, and the reaction duration is appropriate, which may be used as a reasonable reaction condition.

Table 1. The influence of the catalyst dosage on the yield^a

Catalyst dosage/(mol)%	Reaction time/min	Yield ^b /%
14.0	451	44.7
16.0	257	40.8
22.0	213	44.8
24.0	117	26.8

^a: T: 132°C, ^b: gas chromatography yield.

2.2.2. The Influence of the Reaction Ending Temperature on the Yield

Because of the presence of olefin-forming side reactions, the optimal reaction temperature range must be maintained to avoid side reactions. To investigate how the reaction yield varied, different reaction ending temperatures were tried while the catalyst concentration remained constant at 22.0 percent. The results are displayed in Table 2.

Table 2. The influence of the reaction ending temperature on the reaction yield^a

Reaction time/min	Ending temperature/°C	Content of ether ^b /%	Yield ^c /%
213	132	54.2	44.8
240	134	59.6	46.9
230	137	67.1	46.2
253	145	69.4	28.5

^a: T: 132°C, catalyst concentration:22%(mol); ^b: before distillation detected by gas chromatography; ^c: gas chromatography yield

It is found that the content of di-*n*-butyl ether increased clearly as the ending temperature raised, but the ultimate yield did not. Because water separation becomes apparent when the temperature exceeds 127°C (see 2.2), the suitable temperature range for the ether-forming process is 127-137°C. When the reaction ending temperature is 145°C, more white smoke will emit in the later stages of ordinary distillation. The reason for this is that in acidic and high-temperature conditions, di-*n*-butyl ether is easily decomposed into 1-butanol in the later stages of distillation. The elimination reaction of 1-butanol under acidic high-temperature conditions produces butene gas. As a result, when 22.0 percent of the catalyst is utilized, the reaction ending temperature is regulated between 132-137°C to limit the yield loss caused by the decomposition of di-*n*-butyl ether during the distillation process. To complete the experiment in less time, the recommended ending reaction temperature is chosen at 132°C.

2.2.3. The Effect of Heating Rate on the Reaction Yield

The influence of heating rate on the reaction yield was investigated by parallel experiments after determining the appropriate amount of catalyst to be 22.0 percent and the optimal ending reaction temperature to be 132°C. The following experimental results were obtained (Table 3).

The results in Table 3 show that when the amount of catalyst is constant, there is a tendency that as the heating rate reduces, the reaction yield increases. This pattern

illustrates the requirement for a modest heating rate in the early stages. To that purpose, a suitable reflux rate should be used to gradually raise the reaction temperature to enhance the yield. It has been discovered that keeping the reflux at a speed that allows the reflux liquids to drop at a rate of 1-2 droplets per second is appropriate.

Table 3. The effect of heating rate on the reaction yield^a

Entry	temperature changes/K·min ⁻¹	Yield ^b /%
1	0.330	45.5
2	0.338	44.8
3	0.362	42.4
4	0.414	40.4

^a: catalyst concentration: 22%(mol), ending temperature:132°C, ^b: gas chromatography yield

2.2.4. Recovery of the Catalyst

Because the concentrated sulfuric acid used in the traditional di-*n*-butyl ether preparation experiment is removed by washing with water, a significant amount of waste acid is generated. To make the experiment more environmentally friendly, the recovery of catalysts was investigated in this study.

The catalyst was recovered by vacuum distillation and normal distillation, with the results compared. The recovery of the catalyst by vacuum distillation was first explored. The residual liquid in the flask could not crystallize after vacuum distillation, making it difficult to recover the catalyst. In this regard, a computational chemistry analysis was performed to determine the reason for this result, and the calculation results show that 1-butanol and di-*n*-butyl ether can form complexes with *p*-toluenesulfonic acid, and the complexation energies of *p*-toluenesulfonic acid to 1-butanol and di-*n*-butyl ether were 64.6 kJ·mol⁻¹ and 77.0 kJ·mol⁻¹, respectively (Figure 1). It is obvious that di-*n*-butyl ether and 1-butanol form strong hydrogen bonds with *p*-toluenesulfonic acid. The hydrogen bonds between the catalyst and the liquids in the system cannot be broken at vacuum distillation's low temperatures, and the residual liquid has a high proportion of di-*n*-butyl ether and 1-butanol, which influences the crystallization of *p*-toluenesulfonic acid. Furthermore, an azeotrope may be formed by combining di-*n*-butyl ether with 1-butanol, which has a lower boiling point and is difficult to collect in a vacuum distillation.

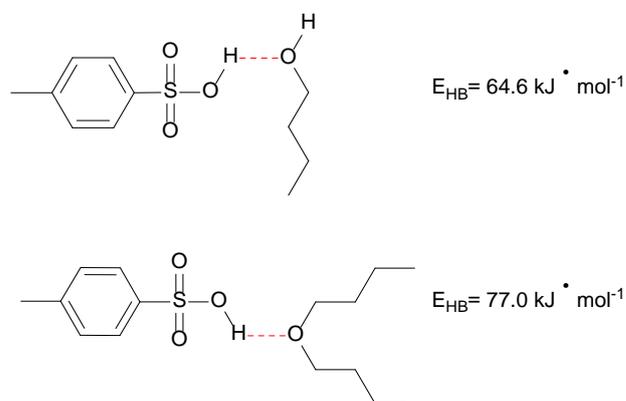


Figure 1. Hydrogen bonding formed in the reaction system (Computational methods: B3LYP/6-31G*, em=GD3BJ//B3LYP/def2-TZVP; SMD, Gaussian 09)

Furthermore, the catalyst was recovered using regular distillation. When the thermometer reading began to fall, the heating was immediately ceased, and the remaining azeotrope comprising 1-butanol and di-*n*-butyl ether was continuously distilled for a while using the residual heat in the flask. Catalyst recovery may be accomplished effectively with this method.

2.3. Reuse of the Catalyst

Under the aforesaid ideal reaction conditions, the recovered *p*-toluene sulfonic acid was reused as a catalyst in a ratio of 22.0 percent (mol). The catalytic effect was shown in Table 4.

The experimental results show that when the recovered *p*-toluenesulfonic acid is reused, the yield of the reaction catalyzed by the secondly used catalyst reduces dramatically as the quality of the first recovered catalyst and the corresponding amount of 1-butanol decreased.

However, based on the di-*n*-butyl ether concentration, the recovered *p*-toluenesulfonic acid retains a high catalytic efficiency. This implies that when the quantity of reactants in the reaction system is sufficient enough, efficient recovery and reuse of *p*-toluenesulfonic acid may be obtained.

Table 4. Catalytic effects of reused catalyst

Entry ^a	Yield ^b /%	Content of ether ^c /%	Recovered catalyst/g
1A	39.8	56.4	6.35
2A	39.0	53.3	-
1B	46.2	67.1	5.75
2B	40.1	79.5	3.67
1C	44.8	54.2	4.59
2C	33.1	65.7	3.35

^a: The recovered catalysts in experiments 1A, 1B, 1C are used in 2A, 2B, and 2C, respectively; ^b: gas chromatography yield; ^c: detected by gas chromatography

Table 5. Comparison of catalytic effects of *p*-toluenesulfonic acid and concentrated sulfuric acid^a

catalyst	dosage of catalyst/(% (mol))	Reaction Ending temperature /°C	Reaction time /min	Yield ^b /%
<i>p</i> -toluenesulfonic acid	22.0	137	230	46.2
concentrated sulfuric acid	27.1	142	97	51.4

^a: 2.00 mL of water is separated in both reactions; ^b: gas chromatography yield.

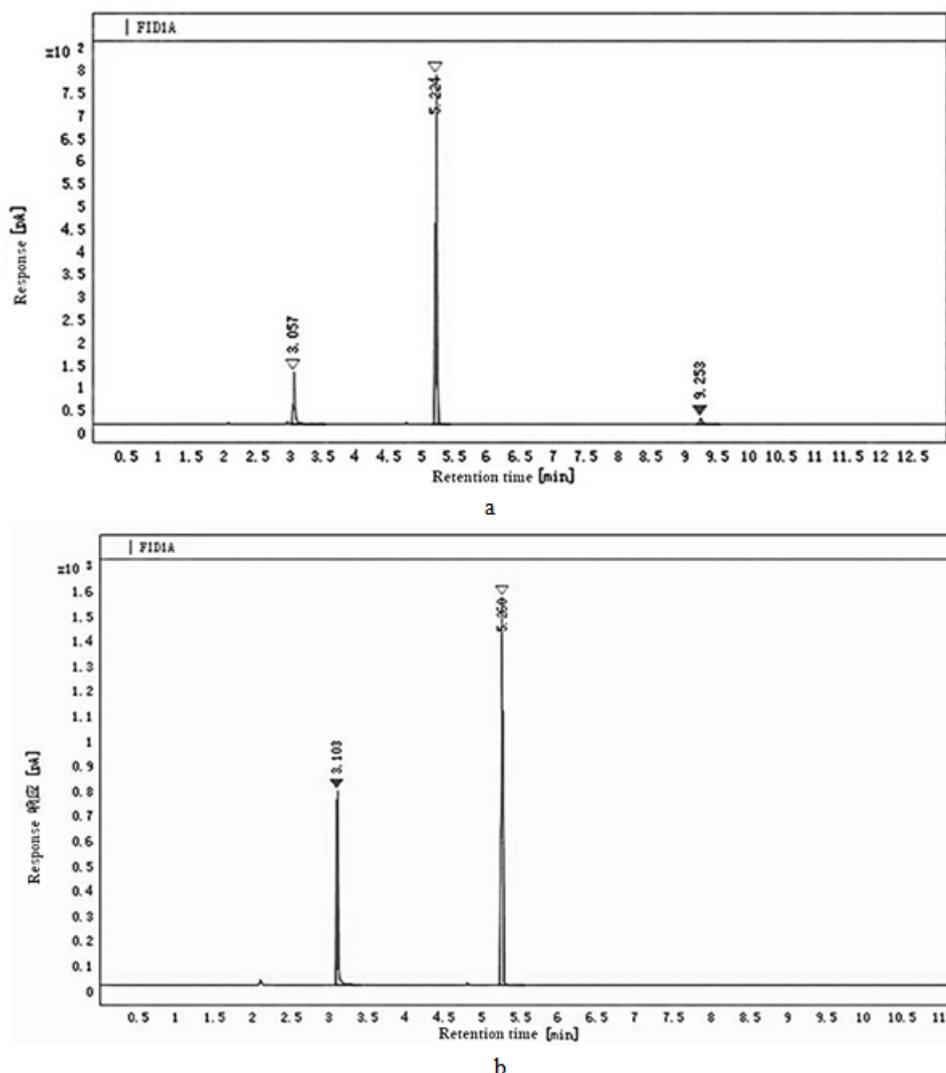


Figure 2. The gas chromatography analysis of the reactants in the ether-forming reaction system

2.4. Product Characterization

Gas chromatography characterization is used to compare the catalytic impact of *p*-toluenesulfonic acid and concentrated sulfuric acid (Table 5, Figure 2). The reaction catalyzed by *p*-toluenesulfonic acid was carried out under the conditions that had been defined to give the highest yield. The reaction catalyzed by concentrated sulfuric acid was carried out under the conditions described in the reference [5].

The initial temperature rise of the chromatographic condition program is 40°C (maintained for 2 minutes), and the temperature is increased to 160°C at a rate of 20°C/min; the auxiliary gas, combustion gas, and auxiliary gas are nitrogen, hydrogen, and air, respectively, with flow rates of 25 and 30 mL/min. The detector and injection port temperatures are both 200°C; split injection, split ratio is 97:1, the injection volume is 0.2 L, capillary column HP-5 (30 m320 m0.25m), column flow rate is 2.0 mL/min.

Figure 2-a shows that the combined solution contains 3.03 percent high-boiling compounds with a retention period of 9.253 minutes. As a result, it can be deduced that concentrated sulfuric acid's strong oxidizing capability leads 1-butanol to oxidize and form high-boiling by-products. To achieve pure di-*n*-butyl ether, forward purification is still required. When *p*-toluenesulfonic acid is employed as a catalyst, on the other hand, a relatively perfect yield may be obtained at a lower reaction temperature, avoiding the formation of high-boiling by-products. As demonstrated in Figure 2-b, no high-boiling by-products are produced in the system, and the distillate requires just a wash with saturated calcium chloride solution to afford di-*n*-butyl ether as the product.

3. Teaching Experiment Design

The operational procedures of the di-*n*-butyl ether preparation experiment have been redesigned based on the findings of this study. The procedure is as follows.

To a 100 mL two-necked round bottom flask, insert a thermometer and a Dean-Stark trap with a water condenser. Then fill the Dean-Stark trap with (V-2) mL of water. Add 15.5 mL of 1-butanol and 7.11g of *p*-toluenesulfonic acid to the flask. Heat the reaction mixture gradually until it boils, and then maintain the reflux at a pace that keeps the reflux liquids falling at a

rate of 1-2 droplets per second. When the reading of the thermometer reaches 132°C, stop heating. Change the reflux equipment to a normal distillation apparatus to collect the fraction at 115-122°C. After distillation, transfer the residual liquid in the distillation flask to a beaker while still hot and cool it down. Wash the resulting solid twice with 10 mL of petroleum ether each time and drain it to recover the catalyst. After washing the distillate with 8 mL of saturated calcium chloride solution, dry it with anhydrous CaCl₂ and filter it to afford the product.

4. Conclusion

In this study, a modification to the experimental preparation of di-*n*-butyl ether from 1-butanol was made by replacing the traditional catalyst of concentrated sulfuric acid with *p*-toluenesulfonic acid, and the catalytic effect of *p*-toluenesulfonic acid was explored. The results show that *p*-toluenesulfonic acid, when being used as a homogeneous catalyst, has a good catalytic impact in the ether-forming process of 1-butanol. It has comparable catalytic efficiency to concentrated sulfuric acid; it can be recovered by regular distillation after the reaction, and it retains excellent catalytic efficiency after further use. As a reusable strong acid with no oxidation or dehydrating properties, *p*-toluenesulfonic acid can be employed as a catalyst in the preparation of di-*n*-butyl ether from 1-butanol instead of concentrated sulfuric acid. This can improve the di-*n*-butyl ether synthesis experiment, which meets the requirements of green chemistry and can be used in the Organic Chemistry Laboratory course.

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