

## Preparation of 4',4''(5'')-Di-*tert*-butyldibenzo-18-crown-6 Based on Electrophilic Aromatic Substitution

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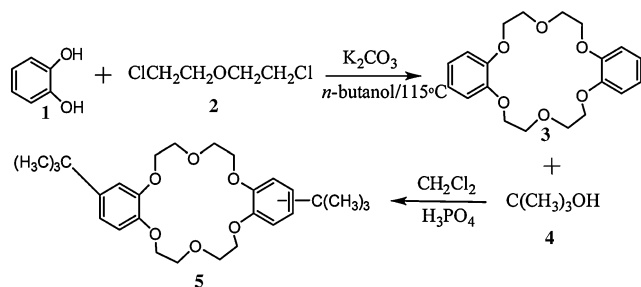
4',4''(5'')-Di-*tert*-butyldibenzo-18-crown-6 (DTBB18C6) was synthesized by improving the electrophilic aromatic substitution of dibenzo-18-crown-6 (DB18C6) using *tert*-butyl alcohol (TBA) as alkylation reagent, H<sub>3</sub>PO<sub>4</sub> (85 wt %) as catalyst and CH<sub>2</sub>Cl<sub>2</sub> as solvent. Experimental results show that the optimized reaction conditions were 0.03 mol L<sup>-1</sup> for TBA concentration, 2.5 for TBA/DB18C6 molar ratio, 0.006 mol L<sup>-1</sup> for H<sub>3</sub>PO<sub>4</sub> concentration, 50 °C reaction temperature, and 6 h reaction time. Under the optimum reaction conditions, DTBB18C6 yield can reach 43.65%.

Nowadays, with the development of the nuclear energy industry, a large volume of high-level nuclear waste (HLW) has been produced and it is necessary to remove <sup>137</sup>Cs from HLW for safe disposal.<sup>1</sup> Among the methods for separating <sup>137</sup>Cs from HLW, liquid extraction has been particularly attractive. For liquid extraction, DTBB18C6 was reported to be an extractant with remarkable ability of complexation and transportation of <sup>137</sup>Cs.<sup>2</sup>

Since Pedersen first synthesized DTBB18C6 in 1967, only a few papers had reported other synthesis methods of DTBB18C6.<sup>3</sup> One of the approaches for the synthesis of alkyldibenzo-crown ethers is based on the electrophilic aromatic substitution of the catechol units of the parent macrocycle. Tashmukhamedova had used this strategy to synthesize DTBB18C6 using TBA and PPA with a yield of 15%.<sup>4</sup>

However, because of the high activity of the *tert*-butyl group, the multi-*tert*-butyl-substituted dibenzo-18-crown-6 is formed easily, which will lead to a low yield of DTBB18C6. The purpose of this article is to improve the DTBB18C6 synthesis process of electrophilic aromatic substitution (S<sub>E</sub>1) by using more proper alkylation reagents, catalysts, and solvents to obtain DTBB18C6 in a better yield.

DTBB18C6 was prepared according to the method shown in Scheme 1. DB18C6 (compound 3, 0.005 mol) was solved in solvents (100 mL). The mixture of *tert*-butyl alcohol (TBA,



Scheme 1. The synthesis procedure of DTBB18C6.

0.010 mol) and H<sub>3</sub>PO<sub>4</sub> (100 mL) were put in a funnel to add dropwise. The reaction was kept 6 h at 60 °C. 500 mL distilled water and 50 mL dichloromethane were added to the reaction mixture. The organic phase was separated and distilled in vacuo. Column chromatography was used to obtain the DTBB18C6 as white crystals. Mp: 105–110 °C; IR ( $\nu_{\max}$ /cm<sup>-1</sup>): 2960, 2871 (C(CH<sub>3</sub>)<sub>3</sub>), 1266 (Ar–O–C), 1216, 1147 (C–O–C), 964, 887, 802 (1,2,4-subst, benzene); <sup>1</sup>H NMR:  $\delta$  0.95–1.42 (18H, s, C(CH<sub>3</sub>)<sub>3</sub>), 3.82–4.26 (16H, m, CH<sub>2</sub>OCH<sub>2</sub>), 6.70–6.98 (6H, m, ArH); Anal. Calcd for C<sub>28</sub>H<sub>40</sub>O<sub>6</sub>: C, 71.2; H, 8.5%. Found: C, 71.16; H, 8.80%.

The DTBB18C6 yield and DB18C6 conversion were defined as follows:

$$\text{DTBB18C6 yield/\%} = \frac{\text{moles of DTBB18C6 formed}}{\text{initial moles of DB18C6}} \times 100\% \quad (1)$$

$$\text{DB18C6 conversion/\%} = \frac{\text{moles of DB18C6 converted}}{\text{initial moles of DB18C6}} \times 100\% \quad (2)$$

where the moles of DTBB18C6 formed, moles of DB18C6 converted, and initial moles of DB18C6 were determined from HPLC of the reaction mixture.

Three-alkylation-reagent effects were studied in this experiment. It was found that there is no remarkable difference in DTBB18C6 yield when different alkylation reagents were used (Figure 1). That is probably due to their similar activities in S<sub>E</sub>1 reaction, when PPA was employed as catalyst.<sup>5</sup> Considering the toxicities of 1-chloro-2-methylpropane and 1-bromo-2-methylpropane, TBA is the desired alkylation reagent.

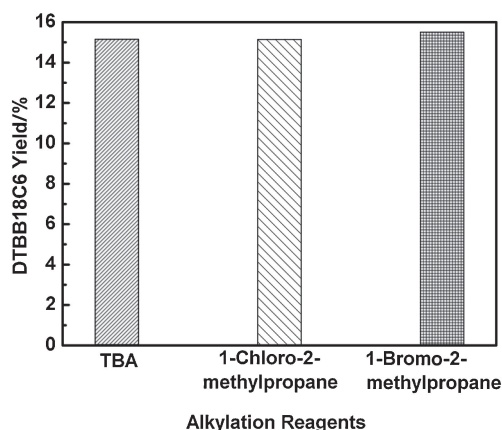
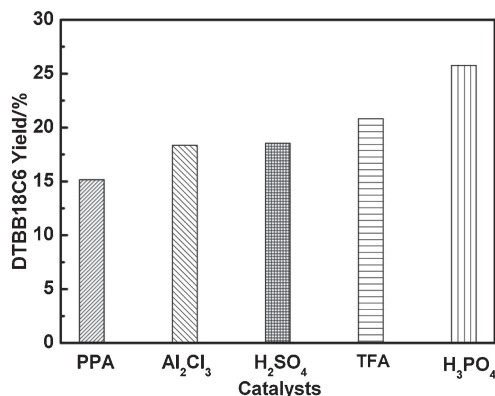
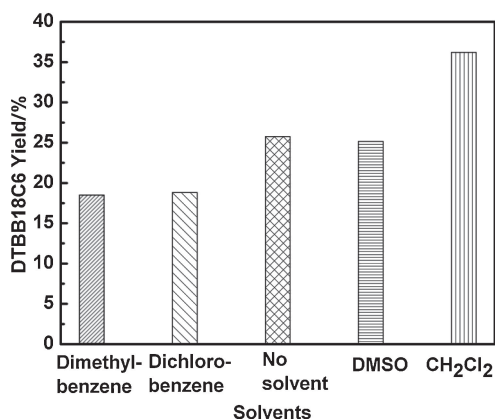


Figure 1. The effect of alkylation reagents on DTBB18C6 yield (PPA as catalyst and no solvent).



**Figure 2.** The effect of catalysts on DTBB18C6 yield (TBA as alkylation reagent and no solvent).

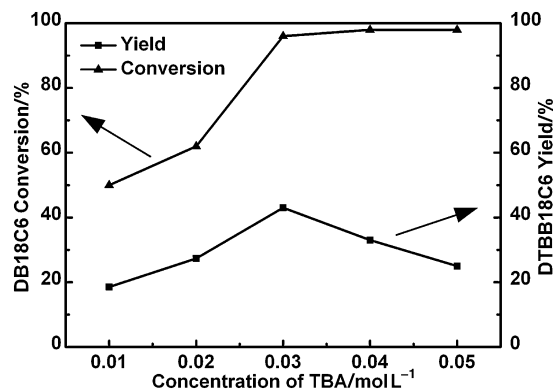


**Figure 3.** The effect of solvents on DTBB18C6 yield (H<sub>3</sub>PO<sub>4</sub> as catalyst and TBA as alkylation reagent).

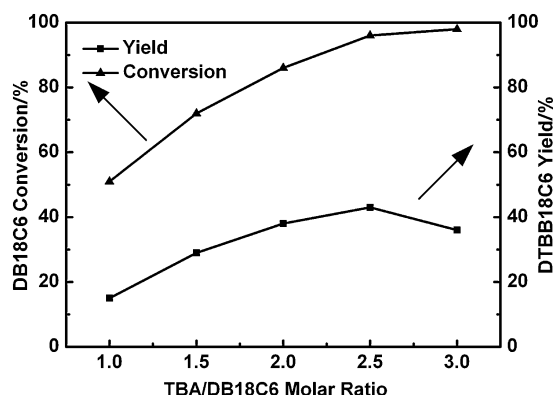
This reaction is an electrophilic aromatic substitution (S<sub>E</sub>1), catalyst is used to react with alkylation reagent to form carbonium ions. Because the higher stability of carbonium ions is helpful to the product yield, it is necessary for catalyst to have more remarkable ability of offering proton.<sup>6</sup> As Figure 2 displayed, the highest yield (25.77%) is found when H<sub>3</sub>PO<sub>4</sub> was employed. It can be explained that H<sub>3</sub>PO<sub>4</sub> as a medium acid has significant ability of offering proton compared with other catalysts. Thus, H<sub>3</sub>PO<sub>4</sub> is believed to be the proper catalyst in this reaction.

In strong polar solvent, the alkylation reagents will be solvated and its efficient concentration will be lower.<sup>6</sup> Poor polar solvent is also harmful for the product yield because the process of the opposite-sign charges separating to form carbonium ions does not occur in poor polar solvent easily.<sup>6</sup> When CH<sub>2</sub>Cl<sub>2</sub> is used as solvent, DTBB18C6 yield increases to 36.21% which is the highest yield in Figure 3. Therefore, CH<sub>2</sub>Cl<sub>2</sub> is the proper solvent with moderate polarity for the synthesis of DTBB18C6.

The changes of DTBB18C6 yield and DB18C6 conversion with TBA concentration are presented in Figure 4. Generally speaking, increasing the concentration of alkylation reagent will increase the product yield too. However, at a higher TBA concentration, DTBB18C6 yield will be result in a fall due to the generation of multi-*tert*-butyl-substituted dibenzo-18-crown-6 in



**Figure 4.** The effect of TBA concentration on DTBB18C6 yield and DB18C6 conversion (H<sub>3</sub>PO<sub>4</sub> concentration: 0.006 mol L<sup>-1</sup>, TBA/DB18C6 molar ratio: 2.5, reaction time: 6 h, reaction temperature: 50 °C).

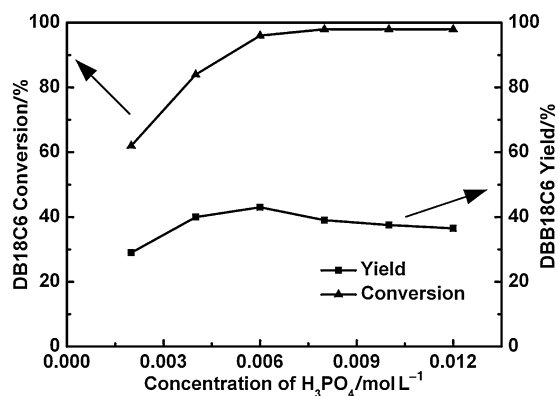


**Figure 5.** The effect of TBA/DB18C6 molar ratio on DTBB18C6 yield and DB18C6 conversion (H<sub>3</sub>PO<sub>4</sub> concentration: 0.006 mol L<sup>-1</sup>, TBA concentration: 0.03 mol L<sup>-1</sup>, reaction time: 6 h, reaction temperature: 50 °C).

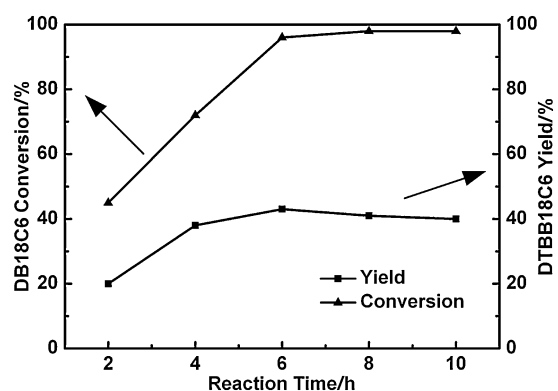
this reaction.<sup>7</sup> The highest DTBB18C6 yield is found when the TBA concentration is 0.03 mol L<sup>-1</sup>, meanwhile the DB18C6 conversion is up to its equilibrium value (96%). DTBB18C6 yield rises quickly at low TBA concentration (less than 0.03 mol L<sup>-1</sup>). When the TBA concentration is higher than 0.03 mol L<sup>-1</sup>, DTBB18C6 yield decreases with the increasing concentration. It shows that increasing the TBA concentration at a low level will promote the reaction process and increase the DTBB18C6 yield.

Further research focusing on the influence of different TBA/DB18C6 molar ratios is needed. The DB18C6 conversion is up to its equilibrium value (96%) in this reversible reaction when the TBA/DB18C6 molar ratio is more than 2.5 (Figure 5). Nevertheless, with the continued increase of TBA/DB18C6 molar ratio the side reaction leading to the synthesis of multi-*tert*-butyl-substituted dibenzo-18-crown-6 will also be enhanced, which gives rise to the decline of the DTBB18C6 yield.<sup>7</sup>

The side reaction will also be enhanced at high concentration of H<sub>3</sub>PO<sub>4</sub>.<sup>6</sup> It may be easier to generate multi-*tert*-butyl-substituted dibenzo-18-crown-6 than DTBB18C6 at high H<sub>3</sub>PO<sub>4</sub> concentration. Figure 6 displays that when the H<sub>3</sub>PO<sub>4</sub> concentration is 0.006 mol L<sup>-1</sup>, DTBB18C6 yield could reach to its



**Figure 6.** The effect of  $\text{H}_3\text{PO}_4$  concentration on DTBB18C6 yield and DB18C6 conversion (TBA concentration:  $0.03 \text{ mol L}^{-1}$ , TBA/DB18C6 molar ratio: 2.5, reaction time: 6 h, reaction temperature:  $50^\circ\text{C}$ ).

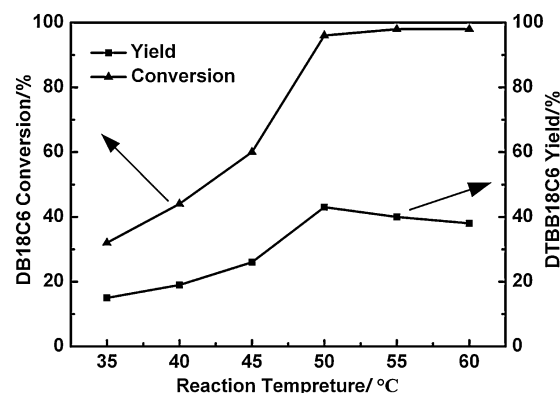


**Figure 7.** The effect of reaction time on DTBB18C6 yield and DB18C6 conversion (TBA concentration:  $0.03 \text{ mol L}^{-1}$ , TBA/DB18C6 molar ratio: 2.5,  $\text{H}_3\text{PO}_4$  concentration:  $0.006 \text{ mol L}^{-1}$ , reaction temperature:  $50^\circ\text{C}$ ).

maximum of 43.65% (Figure 6). The DB18C6 conversion reaches its equilibrium value (96%) when the  $\text{H}_3\text{PO}_4$  concentration is more than  $0.008 \text{ mol L}^{-1}$ .

As with many reversible reactions, extending reaction time will increase the product yield. However, longer reaction time would cause the side reaction of DTBB18C6 with TBA, which will lead to the synthesis of multi-*tert*-butyl-substituted dibenzo-18-crown-6 and a decrease in the DTBB18C6 yield.<sup>6</sup> There is an optimum reaction time (6 h) for DTBB18C6 synthesis, as Figure 7 depicts. DTBB18C6 yield increases straightly until it reaches the highest value (43.65%) in a short reaction time (less than 6 h). When the time exceeds 6 h, DTBB18C6 yield reduces with time. The equilibrium value of DB18C6 conversion appears at about 6 h. It can be easily explained that with the time increase, the DTBB18C6 will reach its equilibrium yield gradually. Hence it is important to control the reaction time strictly.

Alkylation is an exothermic reaction, and the effect of reaction temperature on DTBB18C6 yield is supposed to be that increasing temperature is unfavorable for DTBB18C6 yield when it is at high level. As Figure 8 showed, there is an optimum reaction temperature ( $50^\circ\text{C}$ ) in this reaction.



**Figure 8.** The effect of reaction temperature on DTBB18C6 yield and DB18C6 conversion (TBA concentration:  $0.03 \text{ mol L}^{-1}$ , TBA/DB18C6 molar ratio: 2.5,  $\text{H}_3\text{PO}_4$  concentration:  $0.006 \text{ mol L}^{-1}$ , reaction time: 6 h).

DTBB18C6 yield rises quickly with temperature increasing at low reaction temperature (less than  $50^\circ\text{C}$ ). When the temperature is higher than  $50^\circ\text{C}$ , DTBB18C6 yield declines with the increasing temperature. In addition, equilibrium value (96%) of DB18C6 conversion could be seen when the temperature is more than  $50^\circ\text{C}$ .

TBA is the desired alkylation reagent for its lower toxicity. Increasing the TBA concentration at a low level (less than  $0.03 \text{ mol L}^{-1}$ ) will increase the DTBB18C6 yield. The optimum TBA/DB18C6 molar ratio is about 2.5, and increasing ratio is beneficial to DTBB18C6 yield when the ratio is below 2.5.  $\text{H}_3\text{PO}_4$  has significant ability to offering protons comparing to other acid catalysts, and  $\text{H}_3\text{PO}_4$  is believed to be the proper catalyst for DTBB18C6 synthesis. DTBB18C6 yield increases significantly when  $\text{CH}_2\text{Cl}_2$  is used as solvent. The experimental results also show the optimum reaction temperature and time is  $50^\circ\text{C}$  and 6 h, respectively.

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## References and Notes

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