Reversible Addition and Elimination of Alcohols by Vicinal Tetracarbonyl Compound

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Reversible Addition and Elimination of Alcohols by Vicinal Tetracarbonyl Compound

Shinya Maeda, Atsushi Sudo, Takeshi Endo

Molecular Engineering Institute, Kinki University, Kayanomori 11-6, Iizuka, Fukuoka 820-8555, Japan

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ABSTRACT

In this paper, we report reversible addition and elimination of alcohols by acyclic vicinal tetracarbonyl compound. First, the reversible fixation and release behavior of alcohols by an acyclic vicinal tetracarbonyl compound, 1,4-diphenyl-1,2,3,4-butanetetraone (DPBT) was investigated. On the basis of the results, the addition of alcohol to DPBT was carried out to provide the alcohol adduct of DPBT, which has a hemiacetal structure. Furthermore, we discovered the reaction of DPBT with 2 equivalent amount of methanol.

Introduction

Vicinal tricarbonyl compounds and their reactions have been of interest in the field of organic chemistry. For example, 1,2,3-indanetrione, dehydroascorbic acid, and alloxan are such tricarbonyl compounds, of which reactivity has been investigated.[1,2,3,4,5] Recently, we have focused our attention on 1,3-diphenyl-1,2,3-propanetrione (DPPT), a vicinal tricarbonyl compound with an acyclic structure.[6,7,8] DPPT is a highly electrophilic compound, of which center carbonyl group is activated by the adjacent two carbonyls to be highly reactive with various nucleophiles such as water and alcohols.[9-11] In the course of our investigations on the reactivity of DPPT with alcohols, its equilibrium nature has been clarified.[12] Based on this equilibrium nature, a reversible crosslinking-decrosslinking system using a polystyrene derivative bearing DPPT analogue in the side chain has been constructed.[13]

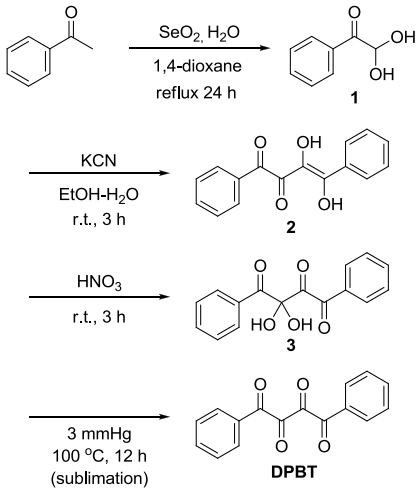
Besides, vicinal tetracarbonyl compounds consisted of four contiguous carbonyl groups have been also an interesting object of research. So far, a couple of 1,4-diaryl-1,2,3,4-butanetetraone have been synthesized and their photo-induced reactions have been investigated.[14] On the other hand, these tetracarbonyl compounds are highly electrophilic similarly to tricarbonyl compounds. For example, 1,4-diphenyl-1,2,3,4-butanetetraone readily reacts with hydroxylamine to afford the corresponding dioxime.[15] 2,2,7,7-Tetramethyl-3,4,5,6-octanetetrone readily reacts with o-phenylenediamine to afford the corresponding quinoxaline.[16]

Herein we report a new aspect of reactivity of 1,4-diphenyl-1,2,3,4-butanetetraone (DPBT). The focus of this report is the reaction behavior of DPBT with a series of alcohols with different steric factors. The most significant finding in this study described herein is the equilibrium nature of the reaction, which would be applicable to construction of reversible polymerization-depolymerization and reversible crosslinking-decrosslinking systems.

*** Corresponding author. Tel.: +81 948 22 7210; fax: +81 94 8 21 9132; e-mail addresses: tendo@moleng.fuk.kindai.ac.jp, tendo@me-jsr.fuk.kindai.ac.jp (T. Endo).**

Result and Discussion

The route for the synthesis of DPBT is depicted in **Scheme 1**[17,18,19]. In the first step, acetophenone was oxidized by selenium dioxide into phenylglyoxal[20]. The second step is the benzoin condensation of phenylglyoxal catalyzed by potassium cyanide, which gave benzoyl formoin. In the third step, benzoyl formoin was oxidized by nitric acid to afford hydrate of DPBT. Heating the hydrate of DPBT at 100 °C in *vacuo* resulted in dehydration and sublimation of DPBT.



Scheme 1. Synthesis of DPBT

The structure of DPBT was confirmed by NMR. In the ^{1}H-NMR spectrum, signals assignable to the phenyl groups were observed (**Figure 1**) (Full spectrum: **Figure S5** in Supporting Information). In the ^{13}C-NMR spectrum of DPBT, the two sequential carbonyl carbon gave two peaks at 188.3 and 186.8 ppm (**Figure S6** in Supporting Information). The IR spectrum showed absorption at 1727, 1664, and 1642 cm^{-1} (**Figure S7** in Supporting Information).

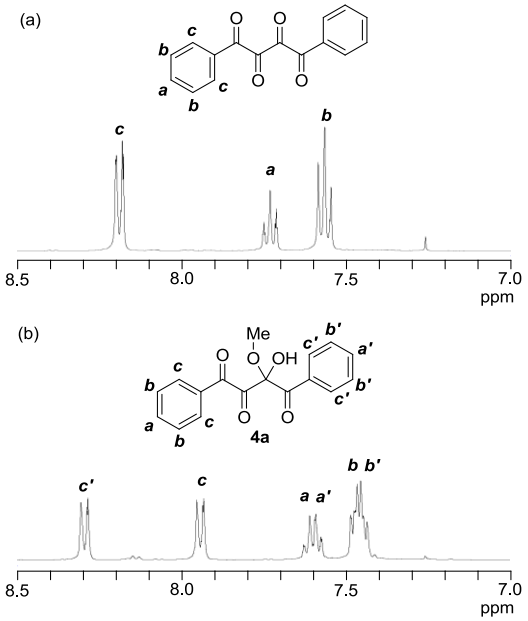
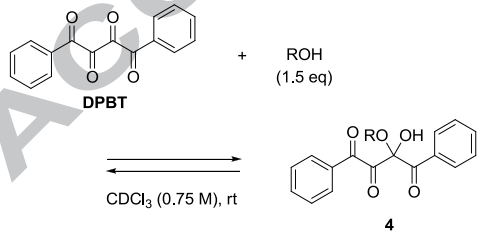


Figure 1. ^{1}H-NMR spectra of DPBT and the reaction mixture of containing adduct **4a**

The reactions of DPBT with various alcohols was investigated (**Scheme 2**). To a 0.75 M solution of DPBT in chloroform-*d* ($CDCl_3$), an equimolar amount of alcohol was added at room temperature, and the resulting solution was analyzed with ^{1}H-NMR spectroscopy to obtain the corresponding time-conversion plots, which are shown in **Figure 2**. During the reactions, the intensities of the signals attributable to the aromatic protons of DPBT decreased, while new signals that implied the formation of adduct **4** gained their intensities. Based on the comparison of the signal intensities, the conversions of DPBT were calculated.



Scheme 2. Reaction behaviors of DPBT with alcohols

First, the reaction of DPBT with methanol was performed. Upon adding methanol to a 0.75 M solution of DPBT in $CDCl_3$, the reaction proceeded smoothly to permit complete consumption of DPBT within 20 min. **Figure 1** shows the ^{1}H-NMR spectrum measured at 20 min after the reaction started. It clarified that DPBT was consumed completely and converted into the corresponding adduct with methanol.

Next, reactions with 1-hexanol and benzyl alcohol were investigated. As shown in **Figure 2**, DPBT reacted with these primary alcohols smoothly but more slowly than the reaction with methanol. Compared to these reactions, the reaction of 2-hexanol, a secondary alcohol with more sterically demanding than the two primary alcohols, was much slower. Besides, DPBT did not react with 2-methyl-2-pentanol, a tertiary alcohol, showing the strong dependence of the reaction efficiency on bulkiness of alcohols.

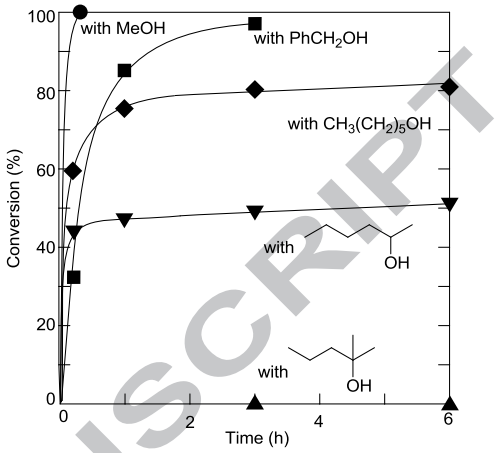
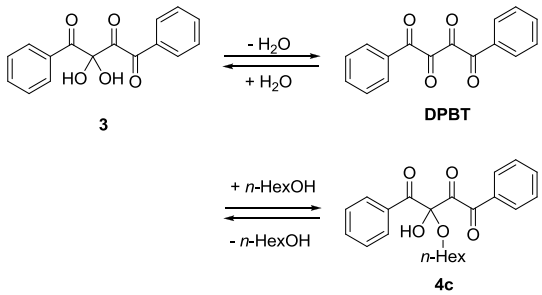


Figure 2. Time-dependences of conversion of DPBT in its reactions with various alcohols in $CDCl_3$ at ambient temperature

In the reactions of DPBT with 1-hexanol and 2-hexanol, the conversions of DPBT plateaued after 1 h, to imply that the reactions reached the equilibriums. This equilibrium nature is analogous to that reported previously for the reaction of 1,3-diphenyl-1,2,3-propanetrione (DPPT) with alcohols. In **Table 1**, the reaction times required for reaching the equilibriums and the conversions at those points in the reactions of DPBT with alcohols are listed. **Table 1** also shows comparative data collected from the time-conversion relationships of the reactions of DPPT with the same alcohols. Comparison of the data for the reactions of DPBT with those for the reactions of DPPT clarified that DPPT was more reactive than DPBT.

Next, the reaction of **3**, a monohydrate of DPBT, with 1-hexanol was investigated (**Scheme 3**). Monohydrate **3** and an equimolar amount of 1-hexanol were dissolved in $CDCl_3$, and the resulting solution was analyzed with ^{1}H-NMR. **Figure 3** shows the obtained ^{1}H-NMR spectra, which confirmed the presences of **3** and **4c** (Full spectrum: **Figure S8** in Supporting Information). In addition, the spectra also revealed the presence of DPBT, which would mediate the inter-conversion between **3** and **4c**. The content ratios of these three compounds were plotted against reaction time (**Figure 4**). Monohydrate **3** was consumed gradually, while the amount of adduct **4c** increased accordingly. DPBT formed immediately in the very early stages and its content ratio did not change significantly throughout the reaction.



Scheme 3. Reversible reactions between monohydrate **3** and DPBT-alcohol adduct **4c**

1.1.

Table 1. Time to reach equilibrium and conversion on DPBT in the addition of various alcohols

Alcohol	Reactions of DPBT with alcohols		Reactions of DPPT with alcohols[a]	
	Time to reach equilibrium (h)	Conversion at the equilibrium (%)	Time to reach equilibrium (h)	Conversion at the equilibrium (%)
Methanol	0.2	100	0.3	100
Benzyl alcohol	3	95	18	80
1-Hexanol	6	81	18	84
2-Hexanol	6	53	64	51

[a] The data are extracted from the previously reported time-conversion relationships[6].

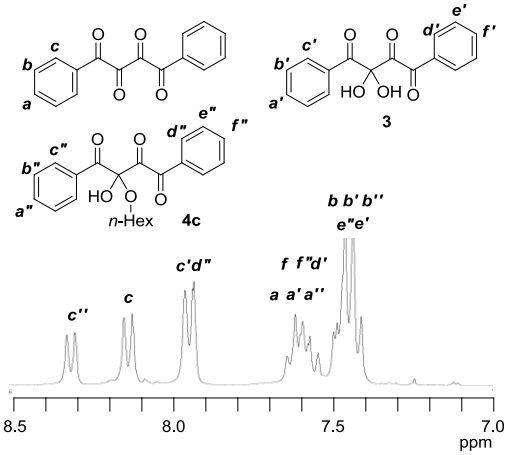


Figure 3. ^{1}H-NMR spectrum of a mixture containing monohydrate **3**, DPBT, and adduct **4a**, formed by the treatment of **3** with 1-hexanol

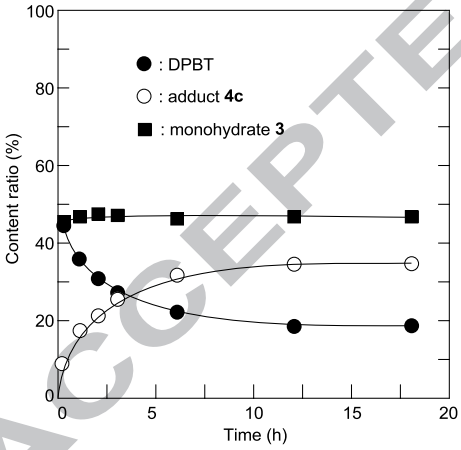
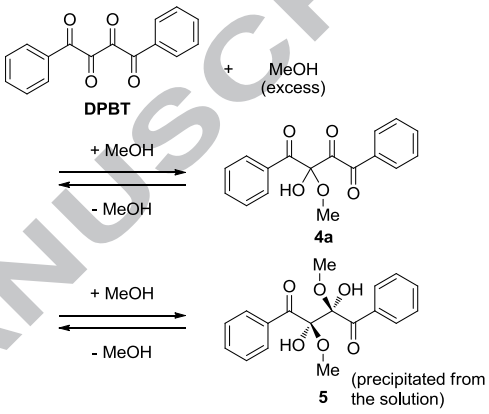


Figure 4. Time-dependences of the content ratios of **3**, **DPBT**, and **4c** upon mixing **3** and hexanol in $CDCl_3$ ([**3**]$_0$:[hexanol]$_0$=0.75 M) at r.t.

These results confirmed that monohydrate **3** and adduct **4c** is in an equilibrium through the formation of DPBT as the intermediate.

Next, DPBT was treated with an excess amount of methanol, with expecting formation of 1:2 adduct of DPBT and methanol (**Scheme 4**). The resulting solution was allowed to stand for 2 weeks, leading to precipitation of a small amount of a white crystal. ^{1}H-NMR and IR analyses of this crystal revealed it was **5**, a 1:2 adduct of DPBT and methanol (Full spectrum showed **Figure S9, Figure S10** in Supporting Information).



Scheme 4. Formation of adduct **5** by the reaction of DPBT with 2 equivalent amount of methanol.

In addition, X-ray crystallography confirmed its structure (**Figure S11** in Supporting Information). When **5** was dissolved in $CDCl_3$ for the structural analysis and kept it at room temperature, the solution colored gradually to yellow. After 20 h, the solution was analyzed by ^{1}H-NMR to find **5** underwent dissociation to form **4a** (**Figure 5**) (Full spectrum: **Figure S12** in Supporting Information). After 60 h, **5** was converted to **4a** almost completely.

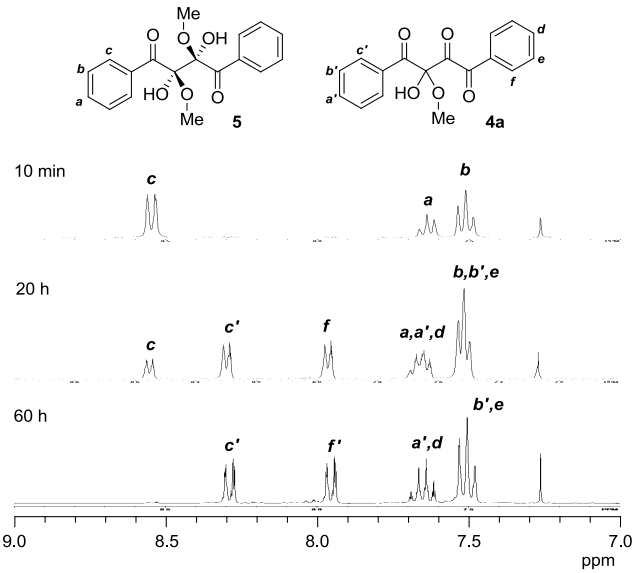


Figure 5. ^{1}H-NMR spectra measured for the dissociation reaction of **5** into **4a** and methanol

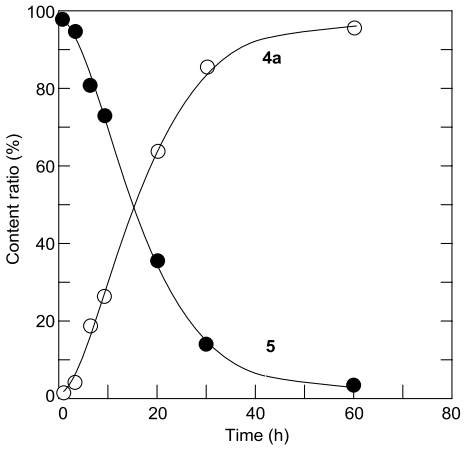


Figure 6. Time dependences of contents of 5 and 4a for the dissociation reaction of **5**

Conclusions

The reaction of 1,4-diphenyl-1,2,3,4-butanetetraone (DPBT), a compound bearing four carbonyl moieties linked linearly, with alcohols was investigated to clarify its equilibrium nature for the first time. DPBT reacted efficiently with primary and secondary alcohols to afford the corresponding mixtures of DPBT-alcohol adducts **4** and DPBT at the equilibriums. The times to reach the equilibriums and the corresponding conversions at the equilibrium were shorter and higher respectively than those observed for the reactions of 1,3-diphenyl-1,2,3-propanetrione (DPPT), a tetracarbonyl compound, investigated previously, to imply the higher electrophilicity of DPBT than DPPT. Based on the equilibrium nature, a reversible system between the monohydrate of DPBT and its adduct with alcohol through the formation of DBPT was constructed. Another interesting reaction discovered in this work was the reaction of DPBT with a two equivalent amount of methanol. The reaction gave the corresponding 1:2 adduct **5a**, which underwent dissociation into 1:1 adduct 4a and methanol. In the present work, chloroform and chloroform-*d* were used as solvents. These solvents can decompose gradually to release HCl and DCl, which may catalyze the reactions, *i.e*., the hydration of DPBT, the addition of alcohols to DPBT, and the dissociations of the adducts. Such catalysis promoting the reactions would be valuable and thus would be investigated in detail in the future work.

The equilibrium nature of the reaction of DPBT with alcohols is potentially applicable to various reversible systems such as reversible polymerization-depolymerization systems and crosslinking-decrosslinking systems that would be useful for chemical recycling of polymer materials.

Measurements.

NMR spectra (400 MHz for ^{1}H; 100.6 MHz for ^{13}C) were recorded on a JEOL NMR spectrometer model JNM-ECS 400 with tetramethylsilane (TMS) as an internal standard. Chemical shift δ and coupling constant J are given in ppm and Hz, respectively. IR spectra were obtained on a Thermo Scientific Nicolet iS10 and wavenumber ν is given in cm^{-1}. Single crystal X-ray analysis was performed on a Bruker Smart ApexCCD-based X-ray diffractometer with Mo−Kα radiation (λ = 0.71073 Å).

EXPERIMENTAL SECTION

Materials.

Chloroform and chloroform-*d* ($CDCl_3$) were distilled and stored on molecular sieves 4A (MS 4A). Methanol, benzyl alcohol, 1-hexanol, 2-hexanol, 2-methyl-2-pentanol were purchased from Sigma-Aldrich Japan and were distilled over CaH_2 prior to use. Selenium dioxide was purchased from Wako Pure Chemical Industries Co., Ltd. and used as received. Acetophenone and potassium cyanide were purchased from Tokyo Chemical Industry Co., Ltd. and used as received. Nitric acid was purchased from Sigma-Aldrich Japan and used as received.

Experimental Section

Reaction of DPBT with alcohols

DPBT (120 mg, 0.450 mmol) was dissolved in dry $CDCl_3$ (0.60 mL) under argon. To the solution, alcohol (0.54 mmol) was added at room temperature. A small portion of the solution was transferred into an NMR tube and analyzed with ^{1}H-NMR to determine conversions of DPBT.

Reaction of 3,3-dihydroxy-1,4-diphenyl-1,2,4-butanetrione (3) with 1-hexanol

Under argon, **3** (129 mg, 0.454 mmol) was dissolved in $CDCl_3$ (0.6 mL). To the solution, 1-hexanol (67.7 μL, 0.54 mmol) was added. A small portion of the solution was transferred into an NMR tube and analyzed with ^{1}H-NMR to determine conversion of **3**.

Synthesis of 2,3-dihydro-2,3-methoxy-1,4-diphenyl-1,4-butanedione (5)

DPBT (120 mg, 4.50 mmol) was dissolved in MeOH (20 mL) under argon. The solution was stirred at room temperature for 2 weeks. The resulting precipitate was collected by filtration with suction to obtain **5** as a colorless crystal (78.7 mg, 0.238 mmol, 5.3 %): ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.09 (s, 6H, OMe), 5.70 (s, 2H, OH), 7.49 (t, *J*=15.5, 4H, Ph), 7.61 (t, *J*=14.7, 2H, Ph), 8.51 (d, *J*=8.7, 4H, Ph). IR(ATR):3397, 1671, 1593, 1575, 1448, 1305, 1241, 1184, 1103, 1052, 992, 966, 941, 873 (**Figure S10** in Supporting Information)

Elimination of methanol from 5

A solution of **5** (5.00 mg, 15.1 mmol) in dry $CDCl_3$ (0.60 mL) was prepared and stored under argon. At designated times, the solution was analyzed with ^{1}H-NMR.

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Graphical Abstract

Reversible Capture and Release of Alcohols by 1,2,3,4-Tetraketone

Shinya Maeda, Atsushi Sudo, Takeshi Endo
Molecular Engineering Institute, Kinki University, Kayanomori 11-6, Iizuka, Fukuoka 820-8555, Japan