



# Short Note 4,4'-(Butane-1,4-diyl)bis(4-methyl-1,2-dioxolane-3,5-dione)

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Abstract: Over the past decades, studies of cyclic diacyl peroxides have shown superior or even fundamentally new reactivity compared to their acyclic counterparts in various reactions. Previously, the scope of cyclic diacyl peroxides was limited to the mono peroxy compounds. The first doubled cyclic diacyl peroxide is presented herein. The diperoxide was characterized by NMR spectroscopy, mass spectrometry, and IR spectroscopy. The structure of 4,4'-(butane-1,4-diyl)bis(4-methyl-1,2dioxolane-3,5-dione) was confirmed by X-ray diffraction analysis. The novel diperoxide was prepared in a 55% overall yield in three steps from dibromobutane and diethyl methylmalonate.

Keywords: peroxides; cyclic diacyl peroxide; oxidants; oxidative coupling

## 1. Introduction

Cyclic diacyl peroxides are compounds with a five- to six-membered rings containing a C(O)-O-C(O) moiety. The chemistry of cyclic diacyl peroxides, first synthesized in the 1950s [1,2], has been actively studied in the last decade [3,4]. Due to their O-electrophilic nature, cyclic diacyl peroxides provide an umpolung approach for the introduction of OR- moiety into organic molecules as an electrophilic "+OR" synthon instead of the usual nucleophilic "-OR" species. The methods for the dihydroxylation, deoxygenation [5–11], and oxyamination [12] of alkenes were developed. Using cyclic diacyl peroxides, the oxyfunctionalization of arenes [13–19], as well as arene dearomatization [20], were achieved. The oxidative acyloxylation of dicarbonyl compounds [21–23], heterocycles [24], and the derivatives of monocarbonyl compounds [25–27] were realized. Such rich reactivity was explained mainly by the weak anomeric  $n_O \rightarrow \sigma^*_{C=O}$  interactions as compared to those in acyclic diacyl peroxides (Scheme 1). Additionally, the transition state in  $S_N^2$  processes with cyclic diacyl peroxides has a more favorable antiperiplanar arrangement of the breaking O-O bond to the  $\sigma^*_{CO}$  bond of the carbonyl [28]. In this work, we presented the doubled cyclic diacyl peroxide 5. One can expect the possibility of synthesizing complex structures of oligomeric and macrocyclic nature using the reactivity of two cyclic diacyl peroxide fragments.



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cyclic diacyl peroxide

weak  $n_0 \rightarrow \sigma^*_{CO}$ anomeric interaction

Scheme 1. Cyclic diacyl peroxides.





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## 2. Results and Discussion

The target peroxide **5** was synthesized in three steps from readily available diethyl methylmalonate **1** and dibromobutane **2** (Scheme 2).

In the first step, diethyl methylmalonate 1 was alkylated with dibromobutane 2 using potassium *tert*-butoxide in DMSO to form tetra ester **3**. After the workup procedure, the crude tetra ester 3 was obtained in almost quantitative yield and was used in the next step without additional purification (Scheme 2). The tetra ester 3 was transformed into tetra acid 4 via base-catalyzed hydrolysis. A typical experimental procedure for relative carboxylic acids includes the acidification of the aqueous solution of the crude carboxylic acid salt and extraction with an organic solvent [29,30]. Because tetra acid 4 is highly soluble in water, extraction is not recommended for isolating the target substance. The isolation procedure of tetra acid 4 included the evaporation of a major volume of a  $CH_3OH/H_2O$ mixture, acidification with conc. HCl, the dissolving of tetra acid 4 in CH<sub>3</sub>CN, filtration from inorganic salts, and the evaporation of organic solvents. Tetra acid 4 was used in the next step without additional purification. The peroxidation of tetra acid 4 with urea hydrogen peroxide in methanesulfonic acid led to doubled cyclic diacyl peroxide 5 in a 55% overall yield in three steps [6,31]. Despite the presence of two peroxide groups, compound 5 is quite thermostable (mp = 113-114 °C without decomposition) and can also be stored in a refrigerator for a year without degradation.



Scheme 2. Three-step synthesis of the doubled cyclic diacyl peroxide 5.

The compound **5** was fully characterized by NMR, IR spectroscopy, and mass spectrometry (Figures S1–S4, Tables S1–S6, Supplementary Materials). The structure of peroxide **5** was confirmed by X-ray diffraction analysis (Figure 1).



Figure 1. The structure of compound 5 obtained by X-ray diffraction analysis.

## 3. Materials and Methods

## 3.1. General Information

Caution: Peroxides are high energy compounds. All reactions using these substances should be conducted within a fume hood and behind a safety-shield. These procedures should be carried out by knowledgeable laboratory workers.

NMR spectra were recorded on commercial instrument (300.13 MHz for <sup>1</sup>H, 75.48 MHz for <sup>13</sup>C) in CDCl<sub>3</sub>. The IR spectrum was recorded with a Bruker (Moscow, Russia) "Alpha-T" instrument in a KBr pellet. High-resolution mass spectrum (HRMS) was measured using electrospray ionization (ESI-TOF) [32]. The measurement was done in a positive ion mode (interface capillary voltage—4500 V); mass range from m/z 50 to m/z 1600 Da; and external/internal calibration was done with Electrospray Calibrant Solution. A syringe injection was used for solutions in CH<sub>3</sub>CN (flow rate 3  $\mu$ L/min). Nitrogen was applied as a dry gas; interface temperature was set at 180 °C.

The TLC analysis was carried out on standard silica gel chromatography plates. The melting point was determined on a Kofler hot-stage apparatus.

X-ray diffraction data were collected at 100 K on a Bruker Quest D8 diffractometer equipped with a Photon III area detector (graphite monochromator, shutterless  $\varphi$ - and  $\omega$ -scan technique), using Mo Ka-radiation. The intensity data were integrated by the SAINT program [33] and corrected for absorption and decay using SADABS [34]. The structure was solved by direct methods using SHELXT [35] and refined on F2 using SHELXL-2018 [36]. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters. The SHELXTL program suite [33] was used for molecular graphics.

#### 3.2. Synthesis of Tetraethyl Octane-2,2,7,7-tetracarboxylate (3)

Potassium *tert*-butoxide (2.96 g, 26.4 mmol) was added to a solution of diethyl 2methylmalonate **1** (4.18 g, 24.0 mmol) in 20 mL of DMSO. After 20 min stirring at 20–25 °C, 1,4-dibromobutane **2** (2.59 g, 12.0 mmol) was added. The resulting suspension was stirred for 5 h at 20–25 °C. The mixture was quenched with H<sub>2</sub>O (50 mL), and the product was extracted with Et<sub>2</sub>O (3 × 40 mL). Combined organic layers were washed with H<sub>2</sub>O (2 × 10 mL), dried over MgSO<sub>4</sub>, and filtered and concentrated under reduced pressure using a rotary evaporator (15–20 mmHg, a water bath temperature ca. 20–25  $^{\circ}$ C) to yield **3** (4.54 g) as a yellow oil. Crude product **3** was used in the next step without purification.

#### 3.3. Synthesis of Octane-2,2,7,7-tetracarboxylic Acid (4)

KOH (7.41 g, 132.0 mmol) was added to a solution of the crude product 3 (4.54 g) in 60 mL of CH<sub>3</sub>OH/H<sub>2</sub>O mixture (5:1, *V*/*V*). The resulting solution was stirred for 24 h at 20–25 °C. After that, the reaction mixture was concentrated under reduced pressure using a rotary evaporator (15–20 mmHg, a water bath temperature 60 °C). CH<sub>3</sub>CN (30 mL) was added to the residue, and the mixture was cooled to 0 °C with an ice–water bath. Then, concentrated hydrochloric acid (10.9 M aqueous solution, 142.0 mmol, 13.0 mL) was added dropwise. The mixture was stirred for 10 min and concentrated under reduced pressure using a rotary evaporator (15–20 mmHg, a water bath temperature 60 °C). CH<sub>3</sub>CN (30 mL) was added to the residue to dissolve the crude organic product. The insoluble inorganic solids were filtered and washed with acetonitrile (3 × 15 mL). The filtrate was concentrated under reduced pressure using a rotary evaporator (15–20 mmHg, a vater bath temperature 40 °C) to yield 4 (3.24 g) as a pale yellow solid. Crude product 4 was used in the next step without purification.

#### 3.4. Synthesis of 4,4'-(Butane-1,4-diyl)bis(4-methyl-1,2-dioxolane-3,5-dione) (5)

Compound 4 (3.24 g) was dissolved in  $CH_3SO_3H$  (25 mL), and the solution was cooled to 0 °C with an ice–water bath. Urea hydrogen peroxide (11.28 g, 112.0 mmol) was added portion wise, and the resulting mixture was stirred for 24 h at 20–25 °C. After that, the reaction mixture was poured onto 30 mL ice. Cold water (100 mL) was added and stirred, and the precipitate was filtered, washed with water (3 × 10 mL), and dried under reduced pressure until no mass change was observed. The product 5 (1.90 g, 6.60 mmol, and 55% overall yield) was obtained as a white powder, mp 113–114 °C.

<sup>1</sup>H NMR (300.13 MHz, CDCl<sub>3</sub>): δ 1.95–1.86 (m, 4H), 1.56 (s, 6H), and 1.42–1.31 (m, 4H). <sup>13</sup>C{<sup>1</sup>H} NMR (75.48 MHz, CDCl<sub>3</sub>): δ 174.1, 43.8, 35.7, 24.1, and 20.5. IR (KBr),  $\nu$ , cm<sup>-1</sup>: 2974 (C-H), 1840 (C=O), 1796 (C=O), 1468 (C-H), 1387, 1289, 1210, 1136, 1071, 1047, 923, 910, 857 (O-O), 740, 680, 669, 604, and 576. HRMS (ESI-TOF) *m*/*z* [M + Na]<sup>+</sup>. Calcd for [C<sub>12</sub>H<sub>14</sub>O<sub>8</sub>Na]<sup>+</sup>: 309.0581. Found: 309.0583.

## 4. Conclusions

The first doubled cyclic diacyl peroxide was prepared in a 55% overall isolated yield via a three-step synthesis from dibromobutane and diethyl methylmalonate. The synthesis was characterized by simplicity and the availability of the reagents.

**Supplementary Materials:** Figure S1: <sup>1</sup>H NMR spectrum of 4,4'-(butane-1,4-diyl)bis(4-methyl-1,2-dioxolane-3,5-dione) (5); Figure S2: <sup>13</sup>C NMR spectrum of 4,4'-(butane-1,4-diyl)bis(4-methyl-1,2-dioxolane-3,5-dione) (5); Figure S3: IR spectrum of 4,4'-(butane-1,4-diyl)bis(4-methyl-1,2-dioxolane-3,5-dione) (5); Figure S4: HRMS spectrum of 4,4'-(butane-1,4-diyl)bis(4-methyl-1,2-dioxolane-3,5-dione) (5); Table S1: crystal data and structure refinement for 4,4'-(butane-1,4-diyl)bis(4-methyl-1,2-dioxolane-3,5-dione) (5); Table S2: atomic coordinates (×10<sup>4</sup>) and equivalent isotropic displacement parameters (Å<sup>2</sup> × 10<sup>3</sup>) for compound (5). U(eq) is defined as one-third of the trace of the orthogonalized Uij tensor; Table S3: bond lengths [Å] and angles [°] for compound (5); Table S4: anisotropic displacement takes the form:  $-2\pi^2$ [h<sup>2</sup> a\* <sup>2</sup>U<sup>11</sup> + ... + 2 h k a\* b\* U<sup>12</sup>]; Table S5: Hydrogen coordinates (×10<sup>4</sup>) and isotropic displacement parameters (Å<sup>2</sup> × 10<sup>3</sup>) for compound (5); Table S6: torsion angles [°] for compound (5).

**Author Contributions:** E.S.G. designed the experiments, prepared the compound, and analyzed the data; V.A.V. supervised the progress of work and wrote the manuscript; A.O.T. designed the study and reviewed and edited the final manuscript to publish. All authors have read and agreed to the published version of the manuscript.

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