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A convenient synthesis of cyclopropane malonyl peroxide

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Cyclopropane-1,1-dicarbonyl peroxide was prepared in 85% yield by the reaction of diethyl cyclopropane-1,1-dicarboxylate with the urea hydrogen peroxide clathrate in the presence of methanesulfonic acid.

Cyclic diacyl peroxide oxidation known since the 1950s[1] has recently undergone a renaissance.[2,3] Cyclopropane malonyl peroxide **1** is the most widely used and the most active oxidizing agent among malonyl peroxides.[2(a),(b),(d),(f),(g)]

The main preparative synthesis of compound **1** is based on the reaction of cyclopropane-1,1-dicarboxylic acid **2** with urea hydrogen peroxide clathrate in the presence of methanesulfonic acid (Scheme 1).[2(a),(f)]

Diacid **2** was prepared in moderate (52–72%) yields in one-pot by alkylation of diethyl malonate with 1,2-dibromoethane in the presence of alkali and a phase-transfer catalyst *via* the stages of formation and hydrolysis of cyclopropane diester **3**.[2(f),4] Higher yield of diacid **2** can be achieved by two-step procedure.[5,6] First, diester **3** was obtained in 92% yield by alkylation of diethyl malonate with 1,2-dibromoethane in the presence of K_2CO_3 and a phase-transfer catalyst. Second, diacid **2** was prepared in high yield by hydrolysis of ester **3**. However, this two-step procedure is more laborious.

Here, we demonstrated that peroxide **1** can be directly prepared in 85% yield by the reaction between diethyl cyclopropane-1,1-dicarboxylate **3** and urea hydrogen peroxide clathrate in the presence of methanesulfonic acid.[†] This reaction is a rare example of the synthesis of peroxides from esters,[7] since peroxides are generally synthesized from acids, anhydrides, or acid chlorides.[8] The method developed in the present study provides an essentially facile approach to the synthesis of peroxide **1**. The reaction can be scaled up to yield gram amounts providing total yield 78% based on diethyl malonate **3**, thus making cyclopropyl malonyl peroxide **1** readily available in laboratory practice.

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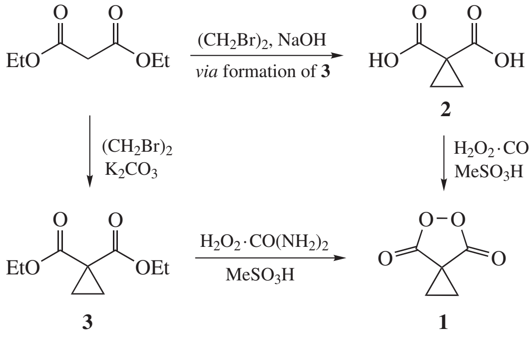

Scheme 1

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[†] *Synthesis of cyclopropane-1,1-dicarbonyl peroxide* **1**. *Caution:* Although we have encountered no difficulties in working with peroxides, precautions, such as the use of shields, fume hoods, and the avoidance of transition metal salts, heating and shaking, should be taken whenever possible.

Urea hydrogen peroxide clathrate (50.80 g, 0.540 mol) was added with stirring to methanesulfonic acid (155.70 g, 105.13 ml), and the mixture was stirred for 2 min. Then diethyl cyclopropane-1,1-dicarboxylate **3** (10.00 g, 0.054 mol) was added, and the mixture was stirred for 24 h. Water (200 ml) and ethyl acetate (200 ml) were added, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (4×50 ml). The combined organic layers were washed with water (2×30 ml), a 5% aqueous $NaHCO_3$ solution (2×30 ml), and again with water (2×30 ml) and dried over $MgSO_4$. The solvent was removed under water jet vacuum. Product **1** was obtained as white crystals in 85% yield (5.88 g, 0.046 mol), mp 89–91 °C (lit.,[2(a)] mp 90 °C). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ: 2.11 (s, 4H). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ: 19.8, 23.6, 172.1.