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In situ generation of hydroperoxide by oxidation of benzhydrols to benzophenones using sodium hydride under oxygen atmosphere: use for the oxidative cleavage of cyclic 1,2-diketones to dicarboxylic acids

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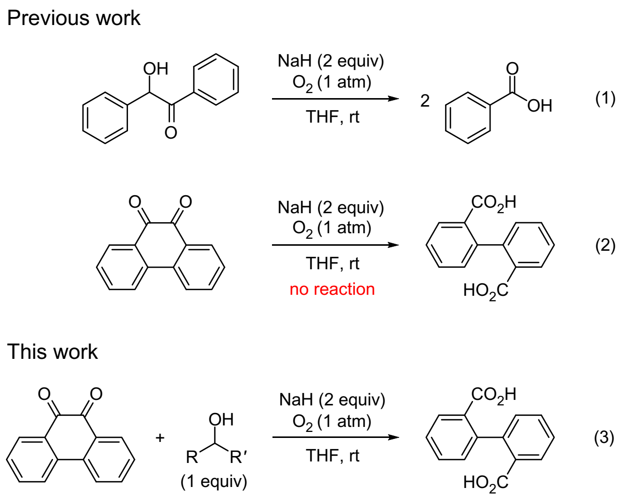
ABSTRACT

A facile oxidative cleavage of cyclic 1,2-diketones **1** to dicarboxylic acids **3** with hydroperoxide generated in situ has been developed. In situ generation of hydroperoxide was effected by the oxidation of 4,4′-dichlorobenzhydrol **2f** to 4,4′-dichlorobenzophenone **4f** using sodium hydride under oxygen atmosphere.

Oxidative cleavage of C–C bonds has emerged as a powerful tool in organic synthesis. Although significant progress has been made in this area, most studies have focused on the oxidative cleavage of C–C double bonds using transition metal catalysts with various co-oxidants. Mostly, such catalysts are based on Mo,[1] W,[2] Mn,[3] Re,[4] Fe,[5] Ru,[6] Os,[7] Pd,[8] and Au.[9] Oxidative cleavage of C–C double bonds is also carried out using ozone[10] or nitric acid.[11] Ochiai and co-workers reported the use of organoiodine reagents for such oxidative cleavage, which is a safer alternative to ozonolysis.[12] Oxidative cleavage of C–C single bonds is relatively less developed compared to that of C–C double bonds. Oxidative cleavage of 1,2-diketones to dicarboxylic acids is one of the few examples, where the C–C single bond is oxidatively cleaved using various oxidizing agents. The oxidants used in such oxidative cleavage are cobaltocene/oxygen,[13] calcium hypochlorite,[14] alkaline hydrogen peroxide,[15] aqueous peracetic acid,[16] sodium percarbonate,[17] and peroxymonosulfate.[18]

Recently, we reported the oxidative cleavage of benzoins to benzoic acids using sodium hydride under oxygen atmosphere (Scheme 1, eq. 1).[19] It was found that hydroperoxide, a key oxidant, was produced upon oxidation of benzoins to benzils and then involved in the subsequent oxidative cleavage of benzils to benzoic acids. Interestingly, however, we observed that the direct oxidative cleavage of benzils (cyclic 1,2-diketones) to benzoic acids (dicarboxylic acids) using NaH and O_2 hardly occurred (Scheme 1, eq.



Scheme 1. Oxidative cleavage reactions attempted using NaH under O_2 atmosphere.

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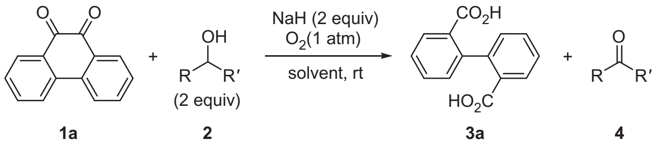
2). This is because hydroperoxide required for such oxidative cleavage is not internally produced when the reaction using NaH and O_2 commences with 1,2-diketones instead of 2-hydroxy ketones. Accordingly, we suggest secondary alcohol/NaH/O_2 as a hydroperoxide equivalent. That is, hydroperoxide can be generated in situ by the oxidation of secondary alcohols to ketones using NaH under O_2 atmosphere. Thus, we reasoned that the oxidative cleavage of 1,2-diketones to dicarboxylic acids would be achieved by using secondary alcohol and NaH under O_2 atmosphere (Scheme 1, eq. 3).

Here, we report the oxidative cleavage of cyclic 1,2-diketones to dicarboxylic acids with hydroperoxide, which was generated in situ by oxidation of benzhydrols to benzophenones using NaH under O_2 atmosphere. Using hydroperoxide thus generated in organic solvent was found to enable such oxidative cleavage to proceed fast and efficiently.

To determine the feasibility of the oxidative cleavage process shown in Eq. 3 of Scheme 1, we first examined the reaction of 9,10-phenanthrenequinone **1a** and 2.0 equiv of 2-propanol **2a** with 3.0 equiv of NaH under O_2 atmosphere. Indeed, cyclic 1,2-diketone **1a** was converted into the desired diacid **3a** in reasonable yield (44%) after 0.5 h (Table 1, entry 2). Using 1-phenylethanol **2b**, we obtained the product **3a** in high yield (83%) after 3 h (Table 1, entry 3). To find the best secondary alcohol for such oxidative cleavage, we screened benzhydrol **2c** and its derivatives **2d**–**f** bearing electron-donating and -withdrawing substituents at the *para*-position of the phenyl ring (Table 1, entries 4–7). Among them, *para*-chloro-substituted benzhydrol **2f** gave diacid **3a** in high yields (83%) within 0.5 h (Table 1, entry 7). On the other hand, the reaction was sluggish when *para*-methoxy-substituted benzhydrol **2d** was employed (Table 1, entry 5). For further optimization of the reaction condition, solvents and the loading of NaH were investigated (Table 1, entries 8–11). The reaction took place less efficiently in other solvents (Table 1, entries 8–10). Low conversion was also

Table 1
Screening of secondary alcohols **2** and solvents for the oxidative cleavage of phenanthrene-9,10-dione **1a** to biphenyl-2,2′-dicarboxylic acid **3a** using NaH under O_2 atmosphere[a]



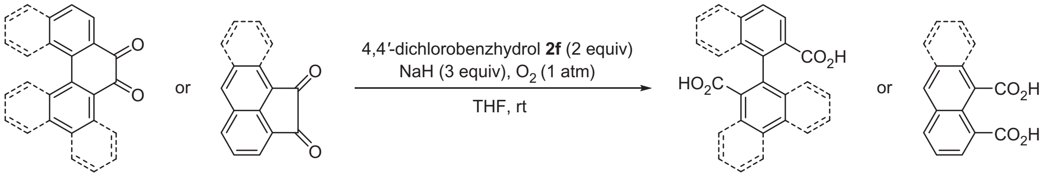
1a **2** **3a** **4**

a. R = R′ = Me
b. R = Ph, R′ = Me
c. R = R′ = Ph
d. R = R′ = 4-$MeOC_6H_4$
e. R = R′ = 4-$F_3CC_6H_4$
f. R = R′ = 4-ClC_6H_4

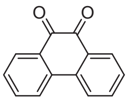
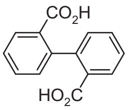
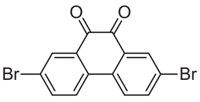
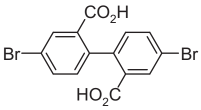
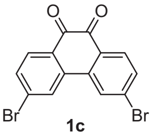
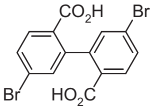
Entry	Alcohol[b]	Solvent	Time (h)[c]	Yield[d] (%)	
				3a[e]	**4**[e]
1	–	THF	24	nd[f]	–
2	**2a**	THF	0.5	44	nd[g]
3	**2b**	THF	3	83	15
4	**2c**	THF	1	59	66
5	**2d**	THF	24	67	83
6	**2e**	THF	1	66	43
7	**2f**	THF	0.5	83	97
8	**2f**	DMF	1	43	75
9	**2f**	Toluene	24	44	50
10	**2f**	CH_2Cl_2	24	6	33
11	**2f**	THF	24	61	34

[a] Reaction conditions: phenanthrene-9,10-dione **1a** (0.5 mmol), secondary alcohol **2** (entries 1–10, 1.0 mmol; entry 11, 0.5 mmol), NaH (entries 1–10, 1.5 mmol; entry 11, 1.0 mmol), O_2 (1 atm), THF (10 mL), rt.
[b] Alcohol **2e** was prepared and characterized as described.[20]
[c] Reaction time ($\leqslant$3 h) determined for the complete consumption of **1a**.
[d] Isolated yield.
[e] Products **3a** and **4** were obtained and characterized as described.[21]
[f] Not detectable.
[g] Not determined.

Table 2
Oxidative cleavage of cyclic 1,2-diketones **1** to dicarboxylic acids **3** using 4,4′-dichlorobenzhydrol **2f** and NaH under O_2 atmosphere[a]



1a–f **1g, 1h** **3a–f** **3g, 3h**

Entry	Substrate[b]	Product[c]	Time[d]	Yield[e] (%)
1	 **1a**	 **3a**	30 min	83
2	 **1b**	 **3b**	10 min	92
3	 **1c**	 **3c**	20 min	66