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A Simple and Effective Method for α-Hydroxylation of β-Dicarbonyl Compounds Using Oxone as an Oxidant without a Catalyst

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Oxone has been found to be a highly efficient reagent for the introduction of a hydroxy group at the α position of a variety of β-dicarbonyl compounds in the homogeneous solvent mixture of water and 1,4-dioxane at 60 °C.

Introduction

α-Hydroxy β-dicarbonyl moieties are common structural units in many natural products and pharmaceuticals, for example, kjellmanianone,[1] hamigeran A,[2] (–)-pramanicin[3] and doxycycline.[4] They also serve as starting materials or key intermediates in the synthesis of a variety of natural products.[5] To date, a number of methods have been developed for the preparation of α-hydroxy β-dicarbonyl moieties.[6] Among them, the direct oxidation of readily available β-dicarbonyl compounds is the most convenient and a number of oxidizing agents have been employed for this transformation. Examples include the stoichiometric application of $Pb(OAc)_4$,[7] oxodiperoxymolybdenum(pyridine)hexamethylphosphoramide (MoOPH),[8] *m*-CPBA,[9] oxaziridines[10] and 2-iodoxybenzoic acid (IBX).[11] However, $Pb(OAc)_4$ and MoOPH are toxic agents and the use of *m*-CPBA, oxaziridines and IBX leads to the formation of large quantities of organic by-products that have to be removed by chromatographic techniques. Dimethyldioxirane (DMDO)[12] and H_2O_2[13] can also be used for the oxidation of β-dicarbonyl compounds. These two oxidants are viewed as "green oxidants" because the only by-product from each oxidant in the reaction is acetone or water. On the other hand, the metal-catalysed α-hydroxylation of β-dicarbonyl compounds with molecular oxygen as the oxidant has received much attention.[14]

Oxone is a cheap, safe, stable, and easily handled oxidizing reagent that has found widespread use in organic synthesis.[15] The most impressive use of Oxone is in the efficient preparation of dimethyldioxirane (DMDO), which can epoxidize olefins readily.[16] Oxone is also well known for its oxidation of boron-,[17] nitrogen-,[18] phosphorus-,[19] sulfur-[20] and selenium-containing[21] compounds. More recently, the ability of Oxone has also been demonstrated in the oxidation of alcohols to the corresponding aldehydes and ketones catalysed by TEMPO and nBu_4NBr,[22] the oxidation of aldehydes to the corresponding acids or esters,[23] the deprotection of acetals and *tert*-butyldimethylsilyl ethers,[24] the oxidative cleavage of olefins, alkynes, α- or β-diketones and α-hydroxy ketones,[25] the oxygenation of the C–H bond[26] and the oxidation of iodoarenes to hypervalent iodine compounds.[27] However, to the best of our knowledge, the use of Oxone for the α-hydroxylation of β-dicarbonyl compounds has never been reported before. Herein, we report a simple and effective protocol for the α-hydroxylation of β-dicarbonyl compounds using Oxone as a stoichiometric oxidant under mild conditions without the aid of a catalyst.

Results and Discussion

Initially, the hydroxylation of methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**1a**) at room temperature using 3.0 equiv. of Oxone in the homogeneous solvent mixture of water and acetonitrile (1:3, v/v) was examined. Methyl 2-hydroxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**2a**) was formed in 70% yield with the conversion of **1a** being 75% after 24 h. When the reaction temperature was elevated from room temperature to 60 °C, the reaction was completed within 10 h and afforded **2a** in 87% yield. The effect of volume ratio of water and acetonitrile was then investigated at 60 °C (Table 1). Substrate **1a** was first subjected to 3.0 equiv. of Oxone in acetonitrile alone and the reaction gave little conversion of **1a** due to the poor solubility of Oxone in acetonitrile (Table 1, entry 1). The use of a 1:1 mixture of water and acetonitrile led to the formation of **2a** in 91% yield within 4 h (entry 3). The best result was obtained when a 3:1 mixture of water and acetonitrile was employed, with **2a** being obtained in 94% yield within 2.5 h (entry 4). The reaction was also carried out in water alone, which gave **2a** in 84% yield after 11 h (entry 5).

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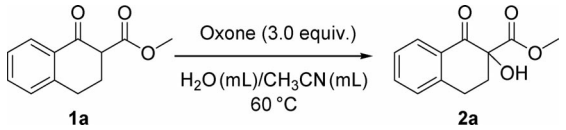
Table 1. The effect of the volume ratio of water and acetonitrile on the hydroxylation of methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**1a**).[a]



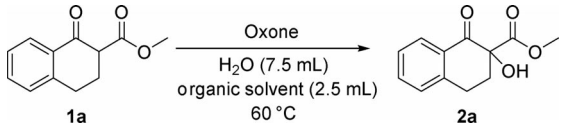
1a **2a**

Entry	H_2O/CH_3CN [mL/mL]	Time [h]	Yield [%][b]
1	0:10	24	20[c]
2	2.5:7.5	10	87
3	5:5	4	91
4	7.5:2.5	2.5	94
5	10:0	11	84[d]

[a] 1 mmol of **1a** was used. [b] Isolated yield. [c] The conversion of **1a** was 21%. [d] The conversion of **1a** was 98%.

A screening study of the amounts of Oxone and organic solvent was then conducted still using **1a** as the model substrate (Table 2). The results shown in Table 2 (Table 2, entries 1–5) indicate that 1.1 equiv. of Oxone are enough for completion of the reaction although a longer reaction time 7 h was required. Among the screened organic solvents, 1,4-dioxane gave the highest yield (98%) within the shortest reaction time (4 h) (entry 6) whereas the use of THF led to little conversion of **1a** (entry 7). The solvent mixtures of water/DMF (3:1, v/v) and water/acetone (3:1, v/v) were also found to be good solvent systems with yields similar to those in water/1,4-dioxane being obtained, but prolonged reaction times were needed (entries 8 and 9 vs. entry 6).

Table 2. Screening of the amounts of Oxone and organic solvents.[a]



1a **2a**

Entry	Oxone [equiv.]	Solvent	Time [h]	Yield [%][b]
1	3.0	CH_3CN	2.5	94
2	2.0	CH_3CN	3.3	95
3	1.5	CH_3CN	5	97
4	1.1	CH_3CN	7	96
5	0.6	CH_3CN	24	90[c]
6	1.1	1,4-dioxane	4	98
7	1.1	THF	26	18[d]
8	1.1	DMF	17	94[e]
9	1.1	acetone	17	96

[a] 1 mmol of **1a** and the indicated amount of Oxone were used. [b] Isolated yield. [c] The conversion of **1a** was 98%. [d] The conversion of **1a** was 19%. [e] The conversion of **1a** was 98%.

A variety of cyclic β-dicarbonyl compounds, including β-keto esters, β-diketones and β-ketoamides, were studied in α-hydroxylation reactions using the optimal reaction conditions (Table 2, entry 6); the results are summarized in Table 3. Methyl 1-oxoindane-2-carboxylate (**1b**) and its two derivatives **1c** and **1d** were readily converted into the corresponding α-hydroxylated products **2b**, **2c** and **2d** in 87, 86 and 80% yields, respectively (Table 3, entries 2–4). The seven-membered-ring-containing substrate **1e** was not a good substrate under the standard conditions in which the desired product **2e** was obtained in only 40% yield with the conversion of **1e** being 48%. However, the use of water/acetonitrile (3:1, v/v) and 3.0 equiv. of Oxone successfully resulted in the formation of **2e** in 70% yield after 24 h (entry 5). The cyclic aliphatic β-keto esters **1f**–**1i** were also readily oxidized to the corresponding desired products **2f**–**2i** in moderate-to-good yields (entries 6–9). Notably, the benzyl group was well tolerated under the reaction conditions (entry 7). For the reactions of β-diketones **1j**–**1o**, both the aromatic and aliphatic β-diketones were efficiently transformed into the corresponding α-hydroxylated β-diketones **2j**–**2o** in good-to-excellent yields (entries 10–15). This new hydroxylation protocol was also effectively applied to β-ketoamides **1p**–**1t** and the reactions provided the expected products **2p**–**2t** in good-to-excellent yields (entries 16–20).

The acyclic substrate ethyl 2-methyl-3-oxo-3-phenylpropanoate (**1u**; Figure 1) was also tested in water/1,4-dioxane (3:1, v/v) and water/acetonitrile (3:1, v/v). The reactions turned out to be too sluggish to be synthetically viable. This is largely the consequence of the lower enol content of **1u** compared with cyclic β-dicarbonyl compounds as the cyclic substrates tend to enolize more readily than the open-chain compounds.[12a,28] Other acyclic substrates including **1v**, **1w**, **1x**, **1y** and **1z** also failed to give the corresponding α-hydroxylated products for similar reasons.[29]

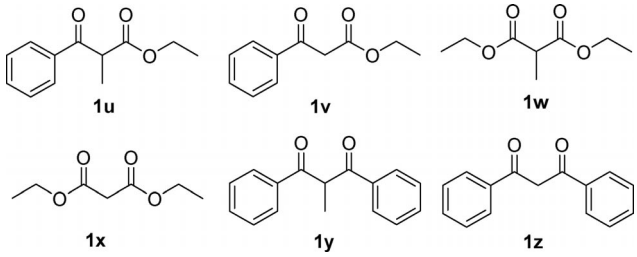
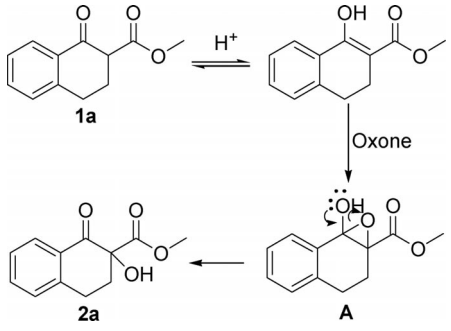


Figure 1. Structures of **1u**–**z**.

It is known that Oxone itself can epoxidize alkenes in aqueous methanol.[30] Thus, as proposed for other hydroxylation reactions,[12a,14e,28] the mechanism for the present transformation may involve the epoxidation of the enol form of **1a** by Oxone to form the hydroxy-epoxide intermediate **A** and subsequent ring-opening to produce the α-hydroxylated β-dicarbonyl compound **2a** (Scheme 1).[31]



Scheme 1. Proposed mechanism for the hydroxylation reaction.

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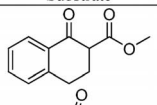
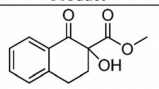
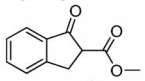
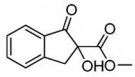
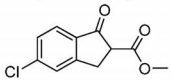
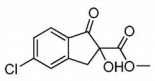
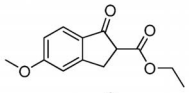
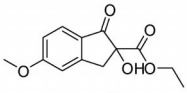
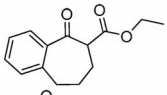
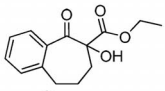
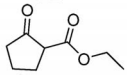
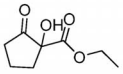
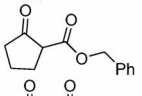
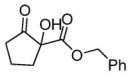
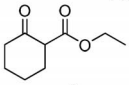
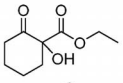
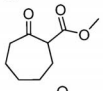
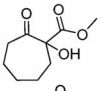
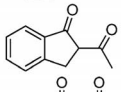
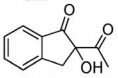
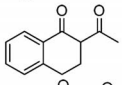
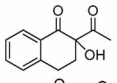
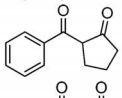
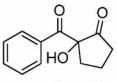
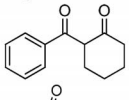
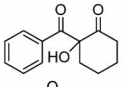
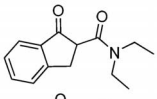
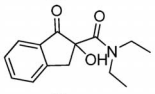
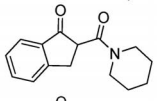
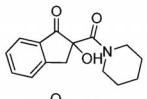
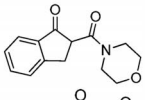
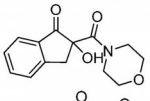
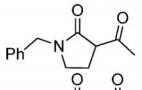
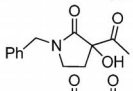
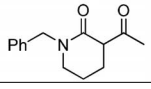
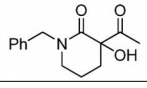
Table 3. α-Hydroxylation of β-dicarbonyl compounds by Oxone.[a]

Entry	Substrate		Product		Time (h)	Yield (%)[b]
1		**1a**		**2a**	4	98
2		**1b**		**2b**	5.5	87
3		**1c**		**2c**	5	86
4		**1d**		**2d**	24	80[c]
5		**1e**		**2e**	24	70[d,e]
6		**1f**		**2f**	22	53
7		**1g**		**2g**	12	65
8		**1h**		**2h**	6	60
9		**1i**		**2i**	16	62[f]
10		**1j**		**2j**	20 min	92
11		**1k**		**2k**	0.5	99
12		**1l**		**2l**	6	71[g]
13		**1m**		**2m**	3	76
14		**1n**		**2n**	0.5	63
15		**1o**		**2o**	0.5	67
16		**1p**		**2p**	11	99
17		**1q**		**2q**	19	98
18		**1r**		**2r**	19	94
19		**1s**		**2s**	7	82[h]
20		**1t**		**2t**	1.5	quant.[h]

[a] Unless otherwise indicated, the reactions were conducted with 1 mmol of β-dicarbonyl compounds and 1.1 mmol of Oxone in a solvent mixture of water and 1,4-dioxane (3:1, v/v) at 60 °C. [b] Isolated yield. [c] The conversion of **1d** was 88%. [d] The reaction was carried out in H_2O/CH_3CN (3:1, v/v) using 3.0 mmol of Oxone at 60 °C. [e] The conversion of **1e** was 82%. [f] The reaction was carried out in H_2O/CH_3CN (3:1, v/v). [g] The reaction was carried out in H_2O/CH_3CN (3:1, v/v) using 2.0 mmol of Oxone at 40 °C. [h] 1.5 mmol of Oxone was used.

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Conclusions

A simple and convenient method for the direct α-hydroxylation of β-dicarbonyl compounds using Oxone as oxidant without a catalyst has been developed. Considering the simplicity and efficiency of the present method, the cost effectiveness, ready availability and ease of handling of Oxone, this method is an attractive method for synthesizing α-hydroxylated β-dicarbonyl compounds.

Experimental Section

General: Oxone was purchased from Alfa Aesar. The known α-hydroxy β-dicarbonyl compounds were identified by comparison of their ^{1}H and ^{13}C NMR spectra with those reported in the literature. The ^{1}H NMR spectra were recorded at 400 MHz and the ^{13}C NMR spectra at 100 MHz using a Bruker AV400 instrument with $CDCl_3$ as solvent. IR spectra were recorded with a FT-IR Bruker EQUINOX55 spectrometer in KBr pellets. High-resolution mass spectroscopy (HRMS) was performed with a high-resolution ESI–FTICR mass spectrometer (Varian 7.0 T). The petroleum ether (PE) used had the range of boiling point 60–90 °C.

Typical Procedure for α-Hydroxylation of β-Dicarbonyl Compounds: Oxone (677 mg, 1.1 mol) was added to a stirred mixture of methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**1a**; 204 mg, 1 mmol) in a mixture of water (7.5 mL) and 1,4-dioxane (2.5 mL) in a 25 mL rounded-bottomed flask at room temperature. The reaction flask was then placed in an oil bath (60 °C) and the reaction was monitored by TLC. After 4 h the reaction mixture was cooled to room temperature and diluted with dichloromethane (50 mL). Then the mixture was washed with satd. aqueous $NaHCO_3$ (10 mL) and satd. aqueous $Na_2S_2O_3$ (10 mL). The separated aqueous phase was extracted with dichloromethane (20 mL) twice. The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo to afford the crude product which was purified by flash column chromatography (PE/EtOAc, 9:1) to give 216 mg of **2a**[14d] in 98% yield as a white solid; m.p. 69–70 °C (ref.[14d] 68 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22–2.29 (m, 1 H, C*H*H), 2.70–2.75 (m, 1 H, CH*H*), 3.12–3.15 (m, 2 H, CH_2), 3.75 (s, 3 H, OCH_3), 4.35 (s, 1 H, O*H*), 7.27 (d, J = 7.6 Hz, 1 H, aromatic C*H*), 7.36 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.54 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 8.05 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 25.52 (CH_2), 32.67 (CH_2), 53.00 (CH_3), 77.66 (C), 126.96 (CH), 128.19 (CH), 128.93 (CH), 130.06 (C), 134.44 (CH), 143.99 (C), 170.99 (CO), 194.54 (CO) ppm.

Methyl 2-Hydroxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2b): (Table 3, entry 2);[32] yield 179 mg (87%); white solid, m.p. 131 °C (ref.[10b] 132–133 °C[10b]). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.19 (d, J = 17.6 Hz, 1 H, C*H*H), 3.68 (d, J = 17.6 Hz, 1 H, CH*H*), 3.67 (s, 3 H, OCH_3), 3.95 (s, 1 H, O*H*), 7.37 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.43 (d, J = 7.6 Hz, 1 H, aromatic C*H*), 7.61 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.73 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 39.23 (CH_2), 53.47 (CH_3), 80.35 (C), 125.33 (CH), 126.46 (CH), 128.16 (CH), 133.49 (C), 136.19 (CH), 152.19 (C), 171.90 (CO), 200.83 (CO) ppm.

Methyl 5-Chloro-2-hydroxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2c): (Table 3, entry 3);[33] yield 206 mg (86%); white solid, m.p. 132–133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.24 (d, J = 17.6 Hz, 1 H, C*H*H), 3.71 (d, J = 17.6 Hz, 1 H, CH*H*), 3.75 (s, 3 H, OCH_3), 4.02 (s, 1 H, O*H*), 7.42 (d, J = 8.0 Hz, 1 H, aromatic C*H*), 7.50 (s, 1 H, aromatic C*H*), 7.74 (d, J = 8.0 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 38.89 (CH_2), 53.63 (CH_3), 80.37 (C), 126.37 (CH), 126.73 (CH), 129.06 (CH), 131.93 (C), 142.85 (C), 153.50 (C), 171.51 (CO), 199.37 (CO) ppm.

Ethyl 2-Hydroxy-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2d): (Table 3, entry 4); yield 200 mg (80%); white solid, m.p. 72–73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, J = 6.8 Hz, 3 H, CH_2CH_3), 3.17 (d, J = 17.2 Hz, 1 H, C*H*H), 3.66 (d, J = 17.2 Hz, 1 H, CH*H*), 3.89 (s, 3 H, OCH_3), 4.02 (br. s, 1 H, O*H*), 4.19 (t, J = 6.8 Hz, 2 H, CH_2CH_3), 6.90 (s, 1 H, aromatic C*H*), 6.93 (d, J = 8.4 Hz, 1 H, aromatic C*H*), 7.71 (d, J = 8.4 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 13.93 (CH_3), 39.22 (CH_2), 55.74 (CH_3), 62.61 (CH_2), 80.56 (C), 109.54 (CH), 116.17 (CH), 126.56 (C), 127.01 (CH), 155.37 (C), 166.34 (C), 171.61 (CO), 198.78 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 3396, 2971, 2945, 2923, 1748, 1698, 1596, 1490, 1466, 1440, 1425, 1389, 1366, 1310, 1269, 1188, 1152, 1090, 1054, 1023, 1006, 935, 893, 846, 657, 558, 495 cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{14}O_5Na$ [M + Na]$^+$ 273.0733; found 273.0739.

6-Ethoxycarbonyl-6-hydroxy-6,7,8,9-tetrahydro-5-oxo-5*H*-benzocycloheptene (2e): (Table 3, entry 5);[14g] yield 174 mg (70%); colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.92–2.09 (m, 3 H, CH_2CHHCH_2), 2.52–2.59 (m, 1 H, CH_2CHHCH_2), 2.86–3.03 (m, 2 H, CH_2CHHCH_2), 4.13 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 4.43 (s, 1 H, O*H*), 7.18 (d, J = 7.6 Hz, 1 H, aromatic C*H*), 7.29 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.42 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.50 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 13.75 (CH_3), 22.65 (CH_2), 33.95 (CH_2), 34.06 (CH_2), 62.04 (CH_2), 81.82 (C), 126.47 (CH), 129.31 (CH), 129.47 (CH), 132.20 (CH), 137.26 (C), 139.86 (C), 170.62 (CO), 204.35 (CO) ppm.

Ethyl 1-Hydroxy-2-oxocyclopentanecarboxylate (2f): (Table 3, entry 6);[14d] yield 91 mg (53%); colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 2.08–2.12 (m, 3 H, CH_2CHHCH_2), 2.44–2.51 (m, 3 H, CH_2CHHCH_2), 3.40 (br. s, 1 H, O*H*), 4.26 (q, J = 7.2 Hz, 2 H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz): δ = 14.01 (CH_3), 18.35 (CH_2), 34.71 (CH_2), 35.80 (CH_2), 62.54 (CH_2), 79.72 (C), 171.56 (CO), 213.37 (CO) ppm.

Benzyl 1-Hydroxy-2-oxocyclopentanecarboxylate (2g): (Table 3, entry 7);[32] yield 152 mg (65%); colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.03–2.15 (m, 3 H, CH_2CHHCH_2), 2.41–2.52 (m, 3 H, CH_2CHHCH_2), 3.80 (s, 1 H, O*H*), 5.16–5.28 (m, 2 H, CH_2), 7.29–7.39 (m, 5 H, aromatic C_5H_5) ppm. ^{13}C NMR (100 MHz): δ = 18.32 (CH_2), 34.66 (CH_2), 35.77 (CH_2), 67.96 (CH_2), 79.84 (C), 126.90 (CH), 128.03 (CH), 128.45 (CH), 128.57 (CH), 128.63 (CH), 134.68 (C), 171.40 (CO), 213.22 (CO) ppm.

Ethyl 1-Hydroxy-2-oxocyclohexanecarboxylate (2h): (Table 3, entry 8):[14d] yield 112 mg (60%); colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.61–1.91 (m, 4 H, $CH_2CH_2CH_2CH_2$), 2.04–2.08 (m, 1 H, $CH_2CH_2CHHCH_2$), 2.53–2.72 (m, 3 H, $CH_2CH_2CHHCH_2$), 4.25 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 4.34 (s, 1 H, O*H*) ppm. ^{13}C NMR (100 MHz): δ = 13.96 (CH_3), 21.94 (CH_2), 27.01 (CH_2), 37.65 (CH_2), 38.86 (CH_2), 62.05 (CH_2), 80.66 (C), 170.06 (CO), 207.28 (CO) ppm.

Methyl 1-Hydroxy-2-oxocycloheptanecarboxylate (2i): (Table 3, entry 9)[13] yield 115 mg (62%); colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.39 (m, 1 H, carbocyclic ring C*H*), 1.46–1.51 (m, 2 H, carbocyclic ring CH_2), 1.81–1.86 (m, 2 H, carbocyclic ring CH_2), 1.97–2.01 (m, 1 H, carbocyclic ring C*H*), 2.10–2.16 (m, 1 H, carbocyclic ring C*H*), 2.24–2.31 (m, 1 H, carbocyclic ring C*H*),

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2.57–2.62 (m, 1 H, carbocyclic ring C*H*), 2.94–3.01 (m, 1 H, carbocyclic ring C*H*), 3.77 (s, 3 H, OCH_3), 4.33 (s, 1 H, O*H*) ppm. ^{13}C NMR (100 MHz): δ = 23.56 (CH_2), 27.21 (CH_2), 30.10 (CH_2), 34.48 (CH_2), 39.84 (CH_2), 53.02 (CH_3), 83.49 (C), 171.03 (CO), 209.49 (CO) ppm.

2-Acetyl-2-hydroxy-2,3-dihydro-1*H*-inden-1-one (2j): (Table 3, entry 10);[32] yield 175 mg (92%); white solid, m.p. 60–61 °C (**2j** was reported as a dark oil in ref.[32]). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08 (s, 3 H, CH_3), 2.26 (d, J = 17.6 Hz, 1 H, C*H*H), 3.64 (d, J = 17.6 Hz, 1 H, CH*H*), 4.54 (s, 1 H, O*H*), 7.48 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.56 (d, J = 7.6 Hz, 1 H, aromatic C*H*), 7.72 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.83 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 23.92 (CH_2), 38.56 (CH_3), 87.16 (C), 125.27 (CH), 126.65 (CH), 128.50 (CH), 134.28 (C), 136.45 (CH), 151.92 (C), 201.42 (CO), 203.67 (CO) ppm.

2-Acetyl-2-hydroxy-3,4-dihydro-2*H*-naphthalen-1-one (2k): (Table 3, entry 11)[32] yield 202 mg (99%); white solid, m.p. 59–60 °C (ref.[14g] 58.5–59.5 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13–2.20 (m, 1 H, C*H*HCH$_2$), 2.26 (s, 3 H, CH_3), 2.55–2.60 (m, 1 H, CH*H*CH$_2$), 3.07–3.10 (m, 2 H, CHHCH_2), 4.74 (s, 1 H, O*H*), 7.23 (d, J = 7.6 Hz, 1 H, aromatic C*H*), 7.31 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.50 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.99 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 24.86 (CH_2), 25.28 (CH_2), 32.11 (CH_3), 81.63 (C), 126.70 (CH), 127.56 (CH), 128.79 (CH), 130.29 (C), 134.29 (CH), 144.01 (C), 196.44 (CO), 206.98 (CO) ppm.

2-Benzoyl-2-hydroxycyclopentanone (2l): (Table 3, entry 12); yield 145 mg (71%); yellow solid, 96–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.99–2.07 (m, 1 H, carbocyclic ring C*H*), 2.10–2.20 (m, 2 H, carbocyclic ring CH_2), 2.43–2.52 (m, 1 H, carbocyclic ring C*H*), 2.61–2.69 (m, 2 H, carbocyclic ring CH_2), 4.14 (s, 1 H, O*H*), 7.46 (t, J = 7.6 Hz, 2 H, aromatic C$_2H_2$), 7.58 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.97 (d, J = 7.6 Hz, 2 H, aromatic C$_2H_2$) ppm. ^{13}C NMR (100 MHz): δ = 17.77 (CH_2), 35.49 (CH_2), 36.07 (CH_2), 85.29 (C), 128.46 (CH), 129.63 (CH), 133.23 (C), 133.54 (CH), 199.92 (CO), 215.81 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 3446, 2986, 2959, 2936, 2874, 2834, 1741, 1663, 1597, 1449, 1439, 1398, 1349, 1319, 1275, 1234, 1171, 1133, 1088, 1058, 1006, 963, 934, 914, 894, 780, 710, 686, 641, 503 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{12}NO_3Na$ [M + Na]$^+$ 227.0679; found 227.0681.

2-Benzoyl-2-hydroxycyclohexanone (2m): (Table 3, entry 13);[11] yield 166 mg (76%); white solid, m.p. 65–66 °C (**2m** was reported as a yellow oil in ref.[11]). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68–1.80 (m, 4 H, carbocyclic ring C$_2H_4$), 2.08–2.12 (m, 1 H, carbocyclic ring C*H*), 2.71–2.76 (m, 2 H, carbocyclic ring CH_2), 2.81–2.84 (m, 1 H, carbocyclic ring C*H*), 4.86 (s, 1 H, O*H*), 7.42 (t, J = 8.0 Hz, 2 H, aromatic C$_2H_2$), 7.54 (t, J = 8.0 Hz, 1 H, aromatic C*H*), 8.04 (d, J = 8.0 Hz, 2 H, aromatic C$_2H_2$) ppm. ^{13}C NMR (100 MHz): δ = 21.87 (CH_2), 27.38 (CH_2), 39.75 (CH_2), 39.96 (CH_2), 84.98 (C), 128.26 (CH), 129.72 (CH), 133.10 (CH), 134.10 (C), 197.78 (CO), 209.93 (CO) ppm.

2-Acetyl-2-hydroxycyclopentanone (2n): (Table 3, entry 14);[32] yield 89 mg (63%); white solid, m.p. 58–59 °C (**2n** was reported as a yellow oil in ref.[32]). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.96–2.05 (m, 1 H, carbocyclic ring C*H*), 2.06–2.14 (m, 2 H, carbocyclic ring CH_2), 2.24 (s, 3 H, CH_3), 2.41–2.47 (m, 3 H, carbocyclic ring CH_2C*H*), 4.23 (s, 1 H, O*H*) ppm. ^{13}C NMR (100 MHz): δ = 17.91 (CH_2), 25.29 (CH_2), 34.28 (CH_2), 35.65 (CH_3), 85.87 (C), 207.30 (CO), 215.14 (CO) ppm.

2-Acetyl-2-hydroxycyclohexanone (2o): (Table 3, entry 15);[14b] yield 105 mg (67%); colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.60–1.76 (m, 2 H, carbocyclic ring CH_2), 1.78–1.91 (m, 2 H, carbocyclic ring CH_2), 2.08–2.11 (m, 1 H, carbocyclic ring C*H*), 2.24 (s, 3 H, CH_3), 2.42–2.46 (m, 1 H, carbocyclic ring C*H*), 2.66–2.72 (m, 2 H, carbocyclic ring CH_2), 4.64 (s, 1 H, O*H*) ppm. ^{13}C NMR (100 MHz): δ = 21.63 (CH_2), 25.47 (CH_2), 27.20 (CH_2), 38.40 (CH_2), 39.35 (CH_3), 85.30 (C), 207.38 (CO), 208.94 (CO) ppm.

***N*,*N*-Diethyl-2-hydroxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxamide (2p):** (Table 3, entry 16); yield 245 mg (99%); white solid, m.p. 60–61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–1.18 (m, 6 H, CH$_2$CH_3CH$_2$CH_3), 2.76–2.87 (m, 2 H, CH_2CH$_3$CH$_2$CH$_3$), 3.23–3.46 (m, 4 H, CH$_2$CH$_3$CH_2CH$_3$, CH_2), 4.55 (br. s, 1 H, O*H*), 7.36–7.43 (m, 2 H, aromatic C$_2H_2$), 7.60 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.78 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 12.39 (CH_3), 12.81 (CH_3), 40.94 (CH_2), 41.10 (CH_2), 41.23 (CH_2), 78.47 (C), 125.22 (CH), 126.87 (CH), 128.29 (CH), 134.17 (C), 135.93 (CH), 151.01 (C), 170.26 (CO), 201.37 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 3547, 3412, 3017, 2976, 2940, 1720, 1638, 1619, 1463, 1381, 1361, 1326, 1301, 1257, 1215, 1186, 1143, 1080, 963, 948, 920, 900, 878, 849, 749, 702, 686, 639, 605, 564, 469 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{17}NO_3Na$ [M + Na]$^+$ 270.1101; found 270.1098.

2-Hydroxy-2-(piperidin-1-ylcarbonyl)-2,3-dihydro-1*H*-inden-1-one (2q): (Table 3, entry 17); yield 254 mg (98%); white solid, m.p. 103–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37–1.59 (m, 6 H, CH$_2$CH_2CH$_2$CH_2CHH), 2.91–2.92 (m, 2 H, CH_2CH$_2$CH$_2$CH$_2$CHH), 3.30 (d, J = 17.6 Hz 1 H, C*H*H), 3.42–3.47 (m, 2 H, CH*H*, CH$_2$CH$_2$CH$_2$CH$_2$C*H*H), 3.80–3.84 (m, 1 H, CH$_2$CH$_2$CH$_2$CH$_2$CH*H*), 4.71 (br. s, 1 H, O*H*), 7.42–7.48 (m, 2 H, aromatic C$_2H_2$), 7.65 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.84 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 24.11 (CH_2), 25.22 (CH_2), 40.83 (CH_2), 44.77 (CH_2), 46.52 (CH_2), 78.27 (C), 125.26 (CH), 126.92 (CH), 128.23 (CH), 133.93 (C), 135.89 (CH), 150.96 (C), 169.20 (CO), 200.92 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 3349, 3069, 3031, 2951, 2854, 1721, 1636, 1608, 1461, 1421, 1368, 1322, 1295, 1279, 1250, 1236, 1206, 1151, 1137, 1125, 1096, 1079, 1046, 1008, 955, 930, 912, 860, 811, 742, 706, 684, 658, 602, 561, 524, 494, 470 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{17}NO_3Na$ [M + Na]$^+$ 282.1101; found 282.1101.

2-Hydroxy-2-(morpholin-4-ylcarbonyl)-2,3-dihydro-1*H*-inden-1-one (2r): (Table 3, entry 18); yield 245 mg (94%); white solid, m.p. 130–132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.23–3.58 (m, 10 H, CH_2, morpholine ring C$_4H_8$), 5.12 (br. s, 1 H, O*H*), 7.37–7.43 (m, 2 H, aromatic C$_2H_2$), 7.60 (t, J = 7.6 Hz, 1 H, aromatic C*H*), 7.77 (d, J = 7.6 Hz, 1 H, aromatic C*H*) ppm. ^{13}C NMR (100 MHz): δ = 40.60 (CH_2), 43.75 (CH_2), 46.17 (CH_2), 66.04 (CH_2), 66.71 (CH_2), 78.99 (C), 125.40 (CH), 126.92 (CH), 128.47 (CH), 133.81 (C), 136.16 (CH), 150.69 (C), 169.84 (CO), 201.23 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 3357, 2999, 2863, 1712, 1637, 1609, 1465, 1450, 1419, 1361, 1326, 1361, 1326, 1301, 1245, 1209, 1199, 1186, 1111, 1082, 1048, 1026, 908, 864, 735, 588 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{15}NO_3Na$ [M + Na]$^+$ 268.0944; found 268.0950.

3-Acetyl-1-benzyl-3-hydroxypyrrolidin-2-one (2s): (Table 3, entry 19);[14b] yield 191 mg (82%); white solid, m.p. 83–85 °C (ref.[14b] 84.5 °C).^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.05–2.17 (m, 1 H, C*H*HCHH), 2.29 (s, 3 H, CH_3), 2.40–2.46 (m, 1 H, CH*H*CHH), 3.29–3.32 (m, 2 H, CH_2), 4.42 (d, J = 14.8 Hz, 1 H, CHHC*H*H), 4.55 (d, J = 14.8 Hz, 1 H, CHHCH*H*), 5.01 (s, 1 H, O*H*), 7.22–7.35 (m, 5 H, aromatic C$_5H_5$) ppm. ^{13}C NMR (100 MHz): δ = 24.95 (CH_2), 30.73 (CH_3), 43.38 (CH_2), 47.27 (CH_2), 83.54 (C), 127.82 (CH), 127.97 (CH), 128.75 (CH), 135.10 (C), 171.69 (CO), 207.63 (CO) ppm.

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3-Acetyl-1-benzyl-3-hydroxypiperidin-2-one (2t): (Table 3, entry 20);[14b] yield 247 mg (100%); white solid, m.p. 101 °C (ref.[14b] 102 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.87–1.94 (m, 3 H, $CH_2CHHCHH$), 2.14–2.24 (m, 1 H, $CH_2CHHCHH$), 2.31 (s, 3 H, CH_3), 3.23–3.33 (m, 2 H, CH_2), 4.49 (d, J = 13.2 Hz, 1 H, $CH_2CHHCHH$), 4.65 (s, 1 H, O*H*), 4.75 (d, J = 13.2 Hz, 1 H, $CH_2CHHCHH$), 7.27–7.37 (m, 5 H, aromatic C_5H_5) ppm. ^{13}C NMR (100 MHz): δ = 18.55 (CH_2), 24.57 (CH_2), 30.62 (CH_3), 47.02 (CH_2), 50.63 (CH_2), 79.36 (C), 127.63 (CH), 127.89 (CH), 128.72 (CH), 136.11 (C), 169.06 (CO), 208.16 (CO) ppm.

Supporting Information (see also the footnote on the first page of this article): ^{1}H and ^{13}C NMR, IR and HRMS spectra of the α-hydroxy β-dicarbonyl compounds.

Acknowledgments

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[31] One referee of this article believed that the substrates and products may be the possible catalysts in our hydroxylation reactions because Oxone can potentially oxidize the substrates or products to give a dioxirane compound that can be used for the hydroxylation of the β-dicarbonyl compounds. However, it is known that the use of Oxone ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$) for the preparation of dioxirane compounds requires strict pH control within the range of 7–11 (either in situ generated dioxirane or isolated one, see ref.[34]). The high pH value not only enhances the nucleophilicity of Oxone towards ketone to produce the intermediate **B** but also favours the shift of the equi-

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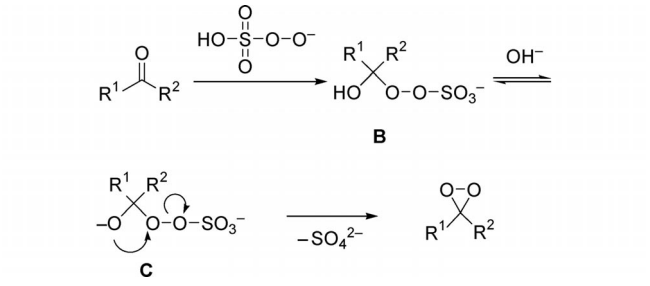
librium (between **B** and **C**) to the formation of intermediate **C**, which can lead to the effective formation of the dioxirane compound.



We tested the acidity of the mixture of Oxone in water/1,4-dioxane (3:1, v/v) by using pH test paper, which indicated that our hydroxylation system was strongly acidic. In this strongly acidic environment, the formation of intermediates **B** and **C** are greatly inhibited. Hence we believe that the dioxirane compound and the Baeyer–Villiger product cannot be formed in our hydroxylation system (in fact neither the dioxirane nor the Baeyer–Villiger products were detected in these hydroxylation reactions). To further exclude the possibility of dioxirane as the active species in our hydroxylation reactions, *trans*-stilbene (an olefin usually used for epoxidation) was treated with 1.0 equiv. of **1a** and 1.1 equiv. of Oxone in a mixture of water and 1,4-dioxane (3:1, v/v) at 60 °C. After 4 h, **1a** was completely converted into **1b** in 95% yield. More importantly, the formation of the epoxide was not observed in the reaction and the *trans*-stilbene was recovered in 98% yield. This result further demonstrated that the dioxirane compound was not formed in our hydroxylation system. Therefore we believe that the mechanism shown in Scheme 1 is still preferable. This referee also suggested that we expand the substrate scope to linear β-dicarbonyl compounds using acetone as the co-solvent. Thus, substrate **1u** was treated with 1.1 equiv. of Oxone in a mixture of water and acetone (3:1, v/v) at 60 °C. The presence of acetone did not improve the efficiency of the reaction with the conversion of the starting material **1u** being only 9% after 24 h. This result also indicates that the dioxirane is not the active species in the hydroxylation reactions.

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