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DBU/O_2-Mediated Oxidation of Dienones

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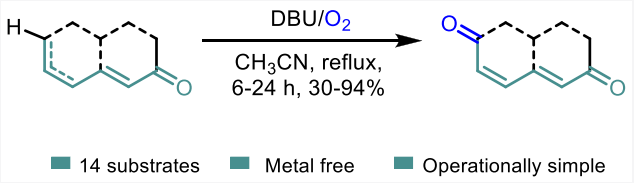
ABSTRACT: Herein, we describe a DBU/O_2-promoted novel method for oxidation of dienones to 2,6-dione derivatives. The reaction involves treatment of a dienone with DBU in acetonitrile employing molecular oxygen as the oxidant. Metal free conditions and an eco-friendly reagent are the striking features of this protocol. This transformation proceeds through a peroxide intermediate that upon Kornblum−DeLaMare rearrangement produces 2,6-diones. The method was successfully utilized for the synthesis of (±)-pleodendione with improved yields versus those of the traditional PDC-TBHP method.



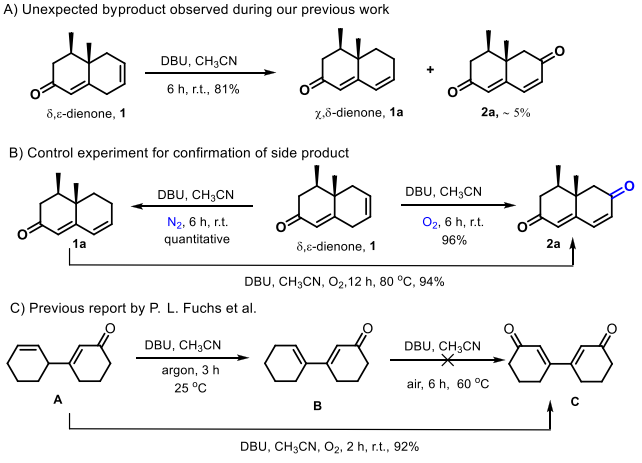
In organic synthesis, the discovery of new methods for allylic oxidation is an ever developing active area. Generally, a double bond present in the system activates the allylic carbon hydrogen bond that aids in the selective installation of the oxygen functionality.[1] These types of reactions are fundamental methods for allylic functionalization and have a great impact on the synthetic chemistry of molecules having commercial value.[2,3] In natural product synthesis, allylic oxidation is greatly important, and to date, a variety of reagents and conditions have been reported. However, there are certain limitations in terms of productivity and chemo- and regioselectivity because of the structural diversity of natural products.

Conventionally, reagents based on chromium(VI) such as pyridinium chlorochromate (PCC), pyridinium dichromate (PDC), PDC-*tert*-butyl hydroperoxide, the CrO_3-pyridine complex, CrO_3 and 3,5-dimethylpyrazole, sodium chromate, sodium dichromate in acetic acid, pyridinium fluorochromate, 3,5-dimethylpyrazolium fluorochromate, and a combination of an *N*-hydroxydicarboxylic acid imide with a chromium-containing oxidant have been used to perform allylic oxidations.[4] Manganese dioxide, potassium permanganate, and selenium dioxide are the other classical methods that use a stoichiometric amount of the reagent.[5] However, these reagents have become less preferred for industrial scale production based on the quantities of reagents required, the volume of solvent used, and tedious workup procedures of the environmentally hazardous metal residues and/or byproducts. Other catalytic methods involve rhodium, iron, copper, cobalt, and palladium as catalysts, most of which are costly, toxic, and avoided in the final stages of API synthesis.[2]

Although various allylic oxidations have been reported in the literature,[6] the development of metal free, eco-friendly synthetic transformations is highly desirable.[7] In this context, while we were working on the synthesis of the peribysin family of natural products,[8] we made an interesting observation when we wanted to perform a double bond migration reaction in compound **1** to obtain compound **1a**.

When the reaction was conducted under the standard protocol using DBU as a base in CH_3CN, we observed compound **2a** in ∼5% yield in addition to expected product **1a** (Scheme 1A). This was quite surprising because no oxidant or metal catalyst was utilized in this reaction. Thus, the only possible oxygen source could be dissolved oxygen from the solvent. To confirm this, we conducted two control experiments, one reaction under a completely inert atmosphere of

Scheme 1. Background



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nitrogen and another reaction in the presence of oxygen. To our delight, the reaction under a nitrogen atmosphere exclusively gave double bond migrated compound **1a** while the reaction under an oxygen atmosphere exclusively furnished oxygenated compound **2a** (Scheme 1B). This experiment confirmed that oxygen acted as an oxidant in this reaction. A similar kind of observation was made by P. L. Fuchs et al. using DBU and oxygen in CH_3CN (Scheme 1C).[9] However, the corresponding conjugated compound (**B**) did not give an oxidized product even after heating at 60 °C. Thus, to confirm this, we applied this method on our substrate **1a** having a conjugated system. At 60 °C, only a trace amount of product was observed, but when the temperature was increased to 80 °C, a 94% yield of the diketo product **2a** was isolated. This unoptimized condition was previously employed by our group for the synthesis of (±)-periconianone A.[10]

Inspired with this result in hand and considering the presence of a naphthalene-2,6-dione skeleton in natural products,[11] we decided to optimize this method and test it with various substrates (selected natural products are captured in Figure 1). For this purpose, compound **1a** was chosen as a

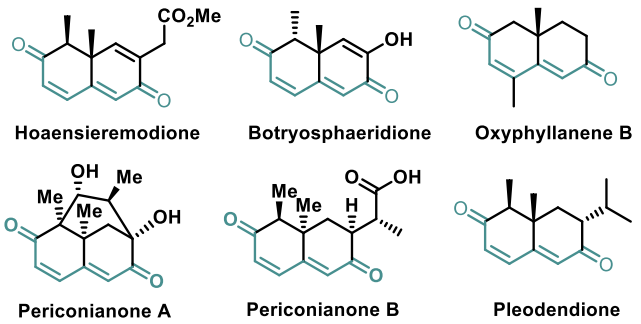

Figure 1. Natural products having 2,6-dione functionality.

model substrate. In our preliminary observations, we obtained desired product **2a** in 46% yield along with <10% formation of 8-hydroxy dienone (**2a′**) and the starting material (**1a**, 45%) was recovered (Table 1, entry 2). To further optimize the reaction condition, we increased the amount of DBU (1.5−2.5 equiv) and observed the formation of **2a** in 94% yield (Table 1, entries 3 and 4). To check the possibility of a further increase in the yield of **2a**, various solvents such as 1,4-dioxane, THF, EtOAc, and DMSO were screened (Table 1, entries 5−8, respectively). The use of 1,4-dioxane and EtOAc as the solvent resulted in a moderate to low yield of **2a**, 49% and 18%, respectively, along with recovery of the starting material (entries 5 and 7, respectively). A trace amount of **2a** was formed in THF, whereas in the case of DMSO, decomposition of the starting material was observed (entries 6 and 8). 1,2-Dichloroethane and toluene gave a low yield of **2a**, while in DMF, the product was not formed (entries 9−11).

Various bases such as NMM, DIPEA, and DABCO were also used for the allylic oxidation reaction (Table 1, entries 12−14, respectively). However, using these bases, no product formation was observed, and only the starting material was recovered. We also tried the reaction of dienone (**1a**) without the use of base, but in that case, only the starting material was recovered (entry 15). Only a trace amount of tetrahydronaphthalene-2,6-dione (**2a**) was observed by oxidation of dienone (**1a**) using Pearlman's catalyst (entry 16). Corey's group has explored this highly selective method for the oxidation of α,β-enones to 1,4-enediones, and very recently, the Wang group reported a highly step and atom economic Pd/Cu combination for accessing 1,4-enediones under aerobic conditions.[12] Therefore, the optimal reaction condition for the preparation of 2,6-dione derivatives (**2a**) was found to be DBU as a base and molecular O_2 as the oxidant in acetonitrile at the reflux temperature.

Considering the importance of this method in total synthesis[12] and to explore the generality of this protocol for the synthesis of 2,6-dione derivatives (**2a**), various dienones (**1**) synthesized using known procedures[13] were examined under the optimized reaction conditions (Table 2). Trienone (**1b**) via the allylic oxidation reaction under optimized conditions gave compound **2b** in a good yield (78%). The oxidation reaction of epimerized trienone and epoxy dienones (**1c** and **1d**) went smoothly to afford the corresponding products (**2c** and **2d**, respectively) in 75% and 44% yields, respectively. The regioselective allylic oxidation of dienones (**1e−h**) having alkenyl, ester, hydroxy alkenyl, and benzyl substituents on a decalin skeleton resulted in good to moderate yields (48−79%) of diketones (**2e−h**). Although the structure of diketone **2h** was proposed on the basis of NMR analysis, it was further confirmed by X-ray analysis (see Table 2 for the ORTEP diagram).

Encouraged by these results in hand, we extended the scope of the reaction to the extended trienone of hexahydroanthracene (**1i**) and found that along with allylic oxidation hydroxylation was observed (**2i**, 52%), which was confirmed by ^1H and ^{13}C NMR in which one of the quaternary carbons at δ 66.5 was observed (no further studies were performed to determine the stereochemistry of the new quaternary center). Additionally, the substrate scope was extended to an alicyclic system such as α-ionone and β-ionone. In both cases, we observed the formation of dione (**2j**) in 76% and 68% yields, respectively. It means α-ionone was converted to β-ionone first and then allylic oxidation occurred.

Similarly, in the case of aliphatic dienone **1k**, the reaction proceeded smoothly to give **2k** in 48% yield. In addition, the reaction of ethyl sorbate and deconjugated ethyl sorbate under optimized conditions gave a moderate yield of the product (**2l**). Here, it is interesting to note that natural product (±)-pleodendione (**2m**) was obtained in 67% isolated yield compared to our previous report using the conventional PDC-TBHP method (46%) (Scheme 2).[13] An ionic mechanism was proposed on the basis of the literature reports and control experiments (see the Supporting Information).[14]

In summary, we have developed a mild and efficient method for the oxidation of dienones to form 2,6-diones, which might find application in the synthesis of natural products and bioactive molecules. Additionally, employing inexpensive DBU as the base and O_2 (balloon) as the oxidant makes this reaction more practical and sustainable. The method was successfully applied for the synthesis of (±)-pleodendione with an improved yield. Further synthetic exploration of this method is underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in oven-dried glassware under a positive pressure of argon or nitrogen unless otherwise mentioned with magnetic stirring. Air sensitive reagents and solutions were transferred via syringe or cannula and introduced into the apparatus via rubber septa. All reagents, starting materials, and solvents were obtained from commercial suppliers and used as such

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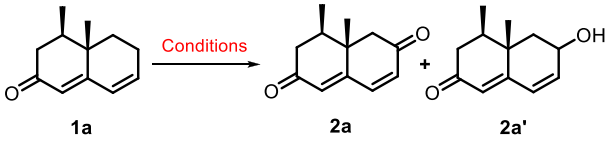
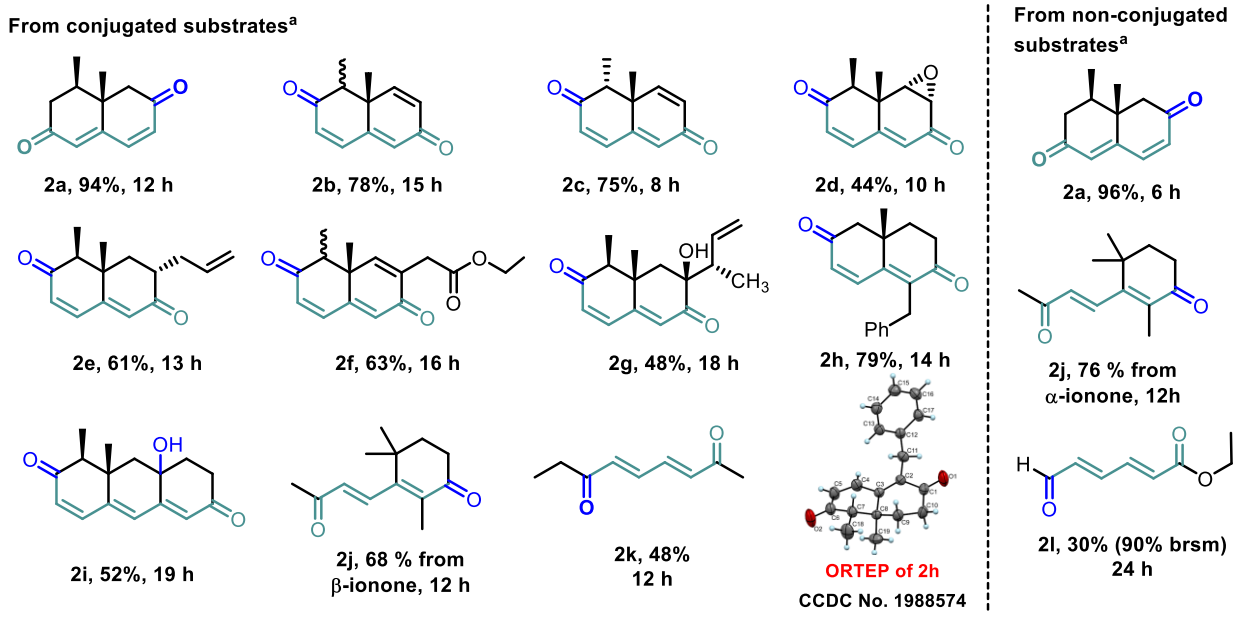
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst/base (equiv)	promoter/oxidant (equiv)	solvent	temp (°C)	time (h)	yield (%)[c] 2a	1a	2a′
1	–	PDC (5)/TBHP (5)	benzene	rt	16	28		–
2	DBU (1.5)	–	CH_3CN	reflux	12	36	45	<10
3	DBU (2.5)	–	CH_3CN	reflux	6	46	32	<5
4	DBU (2.5)	–	CH_3CN	reflux	12	94	ND	ND
5	DBU (2.5)	–	1,4-dioxane	80	12	49	46	<5
6	DBU (2.5)	–	THF	reflux	12	trace	~92	ND
7	DBU (2.5)	–	EtOAc	reflux	12	18	77	trace
8	DBU (2.5)	–	DMSO	80	12		decomposed	
9	DBU (2.5)	–	1,2-DCE	80	12	4	90	ND
10	DBU (2.5)	–	toluene	80	12	9	86	trace
11	DBU (2.5)	–	DMF	80	12		decomposed	
12	NMM (2.5)	–	CH_3CN	reflux	12	trace	90	ND
13	DIPEA (2.5)	–	CH_3CN	reflux	12	ND	98	ND
14	DABCO (2.5)	–	CH_3CN	reflux	12	ND	95	ND
15[b]	–	–	CH_3CN	reflux	12	ND	98	ND
16	$Pd(OH)_2/C$ (0.05), K_2CO_3 (0.5)	TBHP (5)	CH_2Cl_2	rt	12	trace	91	ND

[a]Reaction conditions: dienone (**1a**, 1.0 mmol), catalyst (0.05 mmol) or base (0.5−2.5 mmol) or oxidant (5 mmol) and promoter (5 mmol), solvent (10 mL) stirred at rt to reflux for 6−12 h under an oxygen atmosphere. Abbreviations: PDC, pyridinium dichromate; TBHP, *tert*-butyl hydroperoxide; DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; NMM, *N*-methylmorpholine; DIPEA, *N,N*-diisopropylethylamine; DABCO, 1,4-diazabicyclo[2.2.2]octane; ND, not detected. [b]In the absence of a catalyst or base. [c]Isolated yields.

Table 2. Scope of the Method



[a]The carbonyl group/OH group is from the reaction with DBU, and O_2 is colored blue.

without further purification. Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm precoated silica gel plates (60 F254). Visualization was accomplished either with UV light or by immersion in an ethanolic solution of phosphomolybdic acid (PMA), *p*-anisaldehyde, 2,4-DNP, a $KMnO_4$ solution, or iodine adsorbed on silica gel followed by heating with a heat gun for ~15 s. Column chromatography was performed on silica gel (100−200 or 230−400 mesh). Melting points were determined using a Bruker capillary melting point apparatus and are uncorrected. *S**/*R** nomenclature is used to show the relative stereochemistry of the product. Deuterated solvents for NMR spectroscopic analyses were used as received. All ^1H and ^{13}C NMR spectra were recorded using a Jeol/Bruker 400 MHz or Bruker 500 MHz spectrometer. Coupling constants are reported in hertz. Chemical shifts are quoted in parts per million, relative to TMS, using the residual solvent peak as a reference standard. The following abbreviations were used to explain the

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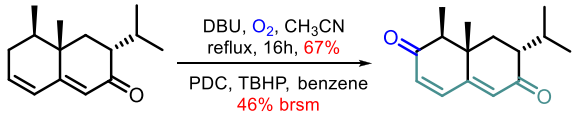
Scheme 2. Synthesis of (±)-Pleodendione



multiplicities: br s, broad singlet; s, singlet; d, doublet; dd, doublet of doublets; t, triplet; td, triplet of doublets; q, quartet; m, multiplet. HRMS (ESI) spectra were recorded on an ORBITRAP mass analyzer (Thermo Scientific, QExactive). Infrared (IR) spectra were recorded on an FT-IR spectrometer as a thin film. The chemical nomenclature was generated using Chem Bio Draw Ultra 14.0.

General Procedure for the Oxidation of Dienones. Into a stirred solution of **1a−m** (1 mmol, 1 equiv) in dry acetonitrile (10 mL) was bubbled oxygen gas for 10 min at room temperature. DBU (2.5 mmol, 2.5 equiv) was added dropwise, and the reaction mixture was refluxed for a period of 6−24 h (using an oil bath as the heating source) under an O_2 atmosphere. The reaction mixture was diluted with ice-cold water (20 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with water, dried over Na_2SO_4, filtered, and concentrated to give the crude product that was purified by column chromatography (ethyl acetate/petroleum ether) to afford **2a−m** in 30−94% yield.

(1R,8aR*)-1,8a-Dimethyl-1,7,8,8a-tetrahydronaphthalene-2,6-dione (**2a**).* Purified by silica gel column chromatography (80:20 petroleum ether/ethyl acetate): isolated yield of 0.122 g, 94%; off-white solid; IR υ_{max} (film) 1655, 1607, 1574, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.05 (dd, J = 0.6, 9.9 Hz, 1 H), 6.20 (d, J = 9.9 Hz, 1 H), 6.08 (s, 1 H), 2.68 (d, J = 15.6 Hz, 1 H), 2.46−2.32 (m, 3 H), 2.26 (dd, J = 4.0, 6.4 Hz, 1 H), 1.17−1.14 (m, 3 H), 1.01 (d, J = 6.5 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.6, 197.8, 158.7, 143.6, 131.6, 129.6, 48.9, 41.7, 39.7, 39.0, 18.4, 14.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_{15}O_2$191.1067, found 191.1064.

*(4R,4aS)-6-Hydroxy-4,4a-dimethyl-4,4a,5,6-tetrahydronaphthalen-2(3H)-one (**2a′**).* Purified by silica gel column chromatography (72:28 petroleum ether/ethyl acetate): isolated yield of 0.148 g; pale yellow liquid; IR υ_{max} (film) 3378, 2958, 1651, 1287, 1041 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.29−6.11 (m, 2 H), 5.79 (s, 1 H), 4.54 (br s, 1 H), 2.39−2.30 (m, 3 H), 2.16−2.04 (m, 1 H), 1.69−1.60 (m, 1 H), 1.07 (s, 3 H), 1.01 (d, J = 6.9 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.5, 161.5, 140.1, 128.5, 125.2, 66.1, 43.1, 41.6, 38.6, 37.9, 16.5, 14.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_{17}O_2$ 193.1228, found 193.1228.

(8aR)-1,8a-Dimethyl-1,8a-dihydronaphthalene-2,6-dione (**2b**) (dr 7:3).* Purified by silica gel column chromatography (75:25 petroleum ether/ethyl acetate): isolated yield of 0.114 g, 78%; colorless solid; IR υ_{max} (film) 2973, 1653, 1625, 1452, 1215 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.11 (m, 1.2 H), 6.82 (d, J = 9.8 Hz, 1 H), 6.53 (s, 0.7 H), 6.45−6.38 (m, 1.2 H), 6.28 (d, J = 9.8 Hz, 0.3 H), 6.17 (d, J = 9.8 Hz, 1 H), 2.67−2.60 (m, 1 H), 1.37 (s, 2 H), 1.35−1.31 (m, 1 H), 1.24 (s, 1 H), 0.94 (d, J = 7.3 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.2, 198.3, 185.8, 185.2, 157.5, 154.8, 154.5, 153.3, 142.5, 142.4, 131.2, 131.0, 129.5, 129.1, 128.9, 128.5, 52.2, 49.5, 45.0, 44.3, 29.6, 28.0, 15.6, 7.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_{13}O_2$ 189.0910, found 189.0907.

(1S,8aR*)-1,8a-Dimethyl-1,8a-dihydronaphthalene-2,6-dione (**2c**).* Purified by silica gel column chromatography (75:25 petroleum ether/ethyl acetate): isolated yield of 0.093 g, 75%; white solid; IR υ_{max} (film) 2974, 1667, 1649, 1618, 1597, 1452, 1307, 1187 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 12.0 Hz, 1 H), 6.81 (d, J = 12.0 Hz, 1 H), 6.53 (s, 1 H), 6.42 (d, J = 12.0 Hz, 1 H), 6.16 (d, J = 12.0 Hz, 1 H), 2.63 (q, J = 8.0 Hz, 1 H), 1.37 (s, 3 H), 0.94 (d, J = 8.0 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.2, 185.9, 154.8, 154.5, 142.5, 131.1, 129.6, 129.1, 52.3, 45.0, 28.1, 15.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_{13}O_2$ $[M + H]^+$ 189.0916, found 189.0925.

(1aR,7R*,7aR*,7bR*)-7,7a-Dimethyl-1a,7,7a,7b-tetrahydronaphtho[1,2-b]oxirene-2,6-dione (**2d**).* Purified by silica gel column chromatography (77:23 petroleum ether/ethyl acetate): isolated yield of 0.045 g, 44%; yellowish oily liquid; IR υ_{max} (film) 2919, 1710, 1676, 1463, 1215, 1094 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, J = 8.0 Hz, 1 H), 6.21 (d, J = 12.0 Hz, 1 H), 6.02 (s, 1 H), 3.68 (d, J = 3.6 Hz, 1 H), 3.48 (dd, J = 3.2, 2.0 Hz, 1 H), 2.74 (q, J = 7.2 Hz, 1 H), 1.36 (s, 3 H), 1.35 (d, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.9, 191.4, 157.1, 142.6, 131.8, 124.4, 60.76, 54.2, 49.3, 40.8, 19.0, 7.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_{13}O_3$ 205.0859, found 205.0858.

(1R,7R*,8aR*)-7-Allyl-1,8a-dimethyl-1,7,8,8a-tetrahydronaphthalene-2,6-dione (**2e**).* Purified by silica gel column chromatography (75:25 petroleum ether/ethyl acetate): isolated yield of 0.094 g, 61%; light yellow solid; IR υ_{max} (film) 2922, 1718, 1665, 1612, 1580, 1388, 1161 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, J = 9.6 Hz, 1 H), 6.22 (d, J = 10.0 Hz, 1 H), 6.05 (s, 1 H), 5.83−5.73 (m, 1 H), 5.12−5.07 (m, 2 H), 2.77−2.72 (m, 1 H), 2.64−2.47 (m, 2 H), 2.21 (dd, J = 14.6, 8.4 Hz, 1 H), 2.14 (dd, J = 13.0, 5.2 Hz, 1 H), 1.70 (t, J = 13.6 Hz, 1 H), 1.17 (s, 3 H), 1.14 (d, J = 6.4 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.8, 199.6, 158.7, 142.1, 135.5, 132.0, 128.8, 117.3, 52.2, 41.4, 40.4, 39.9, 33.5, 18.6, 6.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{19}O_2$ 231.1380, found 231.1378.

Ethyl 2-[(8aR)-8,8a-Dimethyl-3,7-dioxo-3,7,8,8a-tetrahydronaphthalen-2-yl]acetate (**2f**) (dr 7:3).* Purified by silica gel column chromatography (70:30 petroleum ether/ethyl acetate): isolated yield of 0.086 g, 63%; yellowish oily liquid; IR υ_{max} (film) 2976, 1730, 1662, 1632, 1452, 1256, 1163, 1027 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.20 (m, 1 H), 7.03 (s, 0.3 H), 6.73 (s, 0.7 H), 6.55 (s, 0.7 H), 6.45 (s, 0.3 H), 6.28 (d, J = 9.8 Hz, 0.3 H), 6.16 (d, J = 9.8 Hz, 0.7 H), 4.19−4.13 (m, 2 H), 3.48−3.29 (m, 2 H), 2.64 (q, J = 6.7 Hz, 1 H), 1.38 (s, 2 H), 1.33 (d, J = 6.7 Hz, 1 H), 1.29−1.23 (m, 4 H), 0.96 (d, J = 7.3 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.2, 198.3, 184.8, 184.2, 170.7, 170.6, 157.5, 154.8, 152.5, 151.2, 142.3, 142.1, 133.8, 132.7, 131.2, 130.3, 129.1, 128.3, 60.9, 52.4, 49.5, 45.1, 44.3, 34.9, 34.6, 29.6, 27.9, 22.3, 15.5, 14.1, 7.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{19}O_4$ 275.1283, found 275.1292.

(1R,7R*,8aR*)-7-[(R*)-But-3-en-2-yl]-7-hydroxy-1,8a-dimethyl-1,7,8,8a-tetrahydronaphthalene-2,6-dione (**2g**).* Purified by silica gel column chromatography (80:20 petroleum ether/ethyl acetate): isolated yield of 0.089 g, 48%; off-white solid; IR υ_{max} (film) 3412, 1720, 1666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, J = 10.0 Hz, 1 H), 6.25 (d, J = 10.0 Hz, 1 H), 6.18 (s, 1 H), 5.98−5.89 (m, 1 H), 5.22 (d, J = 10.8 Hz, 1 H), 5.16 (d, J = 16.8 Hz, 1 H), 3.49 (q, J = 7.6 Hz, 1 H), 2.79−2.73 (m, 1 H), 2.61 (q, J = 6.8 Hz, 1 H), 2.33 (s, 1 H), 2.06−1.95 (m, 1 H), 1.26 (s, 3 H), 1.18 (d, J = 6.8 Hz, 3 H), 0.95 (d, J = 6.0 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.1, 199.7, 160.5, 141.7, 137.6, 132.4, 127.9, 117.5, 75.5, 52.1, 45.9, 40.3, 39.5, 22.8, 14.6, 7.3; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{16}H_{20}O_3Na$ 283.1305, found 283.1298.

(1R,8aR*)-5-Benzyl-1,8a-dimethyl-1,7,8,8a-tetrahydronaphthalene-2,6-dione (**2h**).* Purified by silica gel column chromatography (70:30 petroleum ether/ethyl acetate): isolated yield of 0.075 g, 79%; colorless solid; IR υ_{max} (film) 2971, 1716, 1663, 1599, 1492, 1453, 1317, 1183 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 10.4 Hz, 1 H), 7.29−7.27 (m, 2 H), 7.21 (d, J = 6.8 Hz, 1 H), 7.14 (d, J = 7.2 Hz, 2 H), 6.23 (d, J = 9.6 Hz, 1 H), 3.89 (s, 2 H), 2.66−2.64 (m, 3 H), 2.13 (d, J = 12.8 Hz, 1 H), 2.04 (dd, J = 12.0, 7.2 Hz, 1 H), 1.23 (s, 3 H), 1.18 (d, J = 6.4 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.9, 197.5, 153.7, 139.4, 139.3, 137.4, 131.5, 128.6 (2C), 127.9 (2C), 126.2, 52.4, 40.9, 33.6, 33.4, 30.3, 17.8, 6.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{21}O_2$ 281.1542, found 281.1544.

(1R,9aR*)-8a-Hydroxy-1,9a-dimethyl-1,7,8,8a,9,9a-hexahydroanthracene-2,6-dione (**2i**).* Purified by silica gel column chromatography (65:35 petroleum ether/ethyl acetate): isolated yield of 0.069 g, 52%; pale yellow solid; IR υ_{max} (film) 3409, 2923, 1647, 1596, 1452, 1323, 1260, 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, J = 9.2 Hz, 1 H), 6.41 (s, 1 H), 6.14 (d, J = 9.6 Hz, 1 H), 5.91 (s, 1 H), 2.89 (td, J = 15.6, 5.2 Hz, 1 H), 2.52 (s, 1 H), 2.48−2.43 (m, 1 H), 2.19 (d, J = 14.8 Hz, 2 H), 2.06 (dd, J = 13.4, 4.4

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Hz, 2 H), 1.71 (d, J = 14.0 Hz, 1 H), 1.34 (s, 3 H), 1.15 (d, J = 6.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.4, 199.4, 153.1, 149.8, 142.8, 129.5, 129.0, 126.5, 66.5, 53.3, 47.2, 40.6, 37.5, 33.1, 20.9, 7.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{19}O_3$ 259.1329, found 259.1327.

*(E)-2,4,4-Trimethyl-3-(3-oxobut-1-en-1-yl)cyclohex-2-en-1-one (**2j**).* Purified by silica gel column chromatography (80:20 petroleum ether/ethyl acetate): isolated yield of 0.146 g, 68%; yellowish oily liquid; IR υ_{max} (film) 2962, 1694, 1666, 1613, 1353, 1312, 1249, 1174 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 16.4 Hz, 1 H), 6.11 (d, J = 16.4 Hz, 1 H), 2.45 (t, J = 7.2 Hz, 2 H), 2.28 (s, 3 H), 1.82 (t, J = 6.8 Hz, 2 H), 1.72 (s, 3 H), 1.12 (s, 6 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.3, 197.2, 157.6, 140.1, 133.4, 131.1, 37.1, 35.3, 33.9, 27.7, 27.1 (2C), 13.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{19}O_2$ 207.1380, found 207.1378.

*Ethyl (2E,4E)-6-Oxohexa-2,4-dienoate (**2k**) (see ref 15 for literature data).* Purified by silica gel column chromatography (70:30 petroleum ether/ethyl acetate): isolated yield of 0.080 g, 48%; yellowish oily liquid; IR υ_{max} (film) 2957, 2853, 1716, 1690, 1642, 1603, 1461, 1367, 1272, 1178, 1095, 1030, 969, 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (d, J = 8.0 Hz, 1 H), 7.42 (dd, J = 15.6, 11.2 Hz, 1 H), 7.17 (dd, J = 15.2, 11.2 Hz, 1 H), 6.43 (dd, J = 15.2, 8.0 Hz, 1 H), 6.31 (d, J = 15.2 Hz, 1 H), 4.27 (q, J = 7.2 Hz, 2 H), 1.33 (t, J = 7.6 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.9, 165.4, 147.2, 140.3, 136.9, 129.9, 61.1, 14.2; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_8H_{10}O_3Na$ 177.0522, found 177.0516.

*(3E,5E)-Nona-3,5-diene-2,7-dione (**2l**) (see ref 16 for literature data).* Purified by silica gel column chromatography (85:15 petroleum ether/ethyl acetate): isolated yield of 0.165 g, 30% (90% brsm); pale yellow liquid; IR υ_{max} (film) 2927, 1678, 1590, 1251 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24−7.08 (m, 2 H), 6.57−6.39 (m, 2 H), 2.64 (q, J = 7.3 Hz, 2 H), 2.33 (s, 3 H), 1.14 (t, J = 7.3 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.2, 197.7, 139.8, 138.6, 136.6, 135.9, 34.5, 29.7, 27.8; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_8H_{10}O_3Na$ 177.0522, found 177.0516.

(1R,7S*,8aR*)-7-Isopropyl-1,8a-dimethyl-1,7,8,8a-tetrahydronaphthalene-2,6-dione (**2m**).* Purified by silica gel column chromatography (78:22 petroleum ether/ethyl acetate): isolated yield of 0.107 g, 67%; colorless oil; IR υ_{max} (film) 2925, 1721, 1665, 1580, 1461, 1386, 1208 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.0 (d, J = 9.6 Hz, 1 H), 6.22 (d, J = 9.6 Hz, 1 H), 6.03 (s, 1 H), 2.65−2.57 (m, 2 H), 2.40−2.34 (m, 1 H), 2.01 (dd, J = 13.0, 4.8 Hz, 1 H), 1.77 (t, J = 13.6 Hz, 1 H), 1.26 (s, 3 H), 1.16 (d, J = 2.4 Hz, 3 H), 1.00 (d, J = 7.2 Hz, 3 H), 0.86−0.84 (m, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.1, 199.9, 158.2, 142.2, 131.9, 129.5, 52.3, 47.2, 40.1, 34.2, 25.8, 20.1, 18.4, 17.6, 7.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{21}O_2$ 233.1536, found 233.1533.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00529.

^1H and ^{13}C NMR spectra of all compounds (PDF)

Accession Codes

CCDC 1988574 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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