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AUTHOR(S):
Kinouchi, Hayate; Sugimoto, Kazuma; Yamaoka, Youseke; Takikawa, Hiroshi; Takasu, Kiyosei

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Oxidative β-Cleavage of Fused Cyclobutanols Leading to Hydrofuran-Fused Polycyclic Aromatic Compounds

Hayate Kinouchi, Kazuma Sugimoto, Yousuke Yamaoka, Hiroshi Takikawa and Kiyosei Takasu*

Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyoku, Kyoto 606-8501, Japan.

E-mail: kay-t@pharm.kyoto-u.ac.jp

Fax: +81 75 753 4604; Tel: +81 75 753 4553

Graphic Abstract
Abstract

Treatment of aryl-fused bicyclo[4.2.0]octanols with an oxidant such as phenyliodine diacetate (PIDA) or hypochlorous acid gave dihydrofuran-containing polycyclic aromatic compounds by selective β-cleavage of the cyclobutanol moiety. Mechanistic studies suggest that the oxygen atom of the hydrofuran ring is incorporated from the hydroxy group of the substrate via intramolecular addition. The oxidative transformation should serve as a new method to prepare functionalized polycyclic aromatic compounds.

Introduction

Polycyclic aromatic hydrocarbons (PAHs) exhibit unique optical and electronic characteristics. PAHs have been applied to electronic devices such as organic light-emitting diodes (OLEDs), organic photovoltaics (OPVs), and organic field-effect transistors (OFETs).1 PAHs are toxic compounds that show carcinogenic and mutagenic effects.2 On the other hand, they have potential as medicinal compounds displaying antitumor activity.3 The size and geometry of the aromatic skeletons and incorporation of heteroatoms into the π-system affect the properties of PAHs. Because introducing functional groups or substituents at peripheral positions can control the properties, a variety of synthetic methods have been reported to prepare functionalized/substituted PAHs.4

We previously reported an intramolecular (2 + 2) cycloaddition of 2-acyl-2′-alkenyl-1,1′-biaryls 1 to furnish diareno-fused bicyclo[4.2.0]octanols 2. This reaction is promoted by a potassium base such as KO′Bu and KHMDS (Scheme 1a).5 We also demonstrated that an acid-promoted retro (2 + 2) cycloaddition of azapropellanes 4 furnishes π-extended carbazoles 5 (Scheme 1c).7 The promotion of these reactions should be driven by alleviating the strain of the cyclobutane rings.8 Oxidative carbon-carbon bond cleaving reactions are valuable synthetic tools, which yield structurally diverse organic molecules. In particular, cyclobutanols are representative substrates for bond cleaving reactions at the β-bond of the hydroxy group. The selectivity of the breaking
β-bond is actively researched.\textsuperscript{9,10} However, most of studies have been done on the oxidative β-cleavage of monocyclic cyclobutanols. The examples for fused cyclobutanols are limited.\textsuperscript{10b,d,f,h} We envisage that an oxidative β-cleavage reaction of diareno-fused bicyclo[4.2.0]octanols 2 gives substituted polyaromatic compounds A or cyclic biaryl compounds B, depending on the breaking C–C bonds (Figure 1). Herein, we describe the synthesis of dihydrofuran-fused PAHs by oxidation of 2 with an unusual regioselective bond cleavage and their further functionalization.

\begin{center}
\textbf{Scheme 1.} Previous works: (a) Potassium base promoted intramolecular (2 + 2) cycloaddition, (b) domino reaction of cyclobutanols 2 giving substituted PAHs 3, (c) retro (2 + 2) cycloaddition of azapropellanes 4 giving tribenzocarbazoles 5.
\end{center}

\begin{center}
\textbf{Figure 1.} This work: Oxidative β-cleavage of diareno-bicyclo[4.2.0]octanols 2. A; A compound resulted in the C(1)–C(2) bond cleavage, B; A compound resulted in the C(1)–C(4) bond cleavage.
\end{center}
Results and Discussion

We initially examined the oxidation of 2a with phenyliodine diacetate (PIDA), which has been used by Fujioka and Kita’s group for β-cleavage of monocyclic cyclobutanols to give γ-hydroxyketones. It was proposed that the reaction proceeds through a cationic pathway. When using the standard reaction in the literature in 1,1,1,3,3,3-hexafluoropropane-2-ol (HFIP) and H2O (9 : 1 v/v), 2a was fully consumed within 1 h to afford 6a in 15% yield (Table 1, entry 1). 1H and 13C {1H} NMR spectra confirmed that 6a had a phenanthrol[9,10-b]furan skeleton. We attributed the low yield of 6a to the overoxidation of the electron-rich phenanthrene ring. Adding PIDA portionwise into the solution of 2a over 15 min increased the yield of 6a to 40% (entry 2). With 1.1 equivalents of PIDA, the yield of 2a was increased into 66% (entry 3).

To suppress the reactivity of PIDA, the solvent was screened. Substituting acidic HFIP as a co-solvent with CH2Cl2 or CH3CN of H2O dramatically improved the yield of 6a to 82% and 97%, respectively (entries 4 and 5). A high yield of 6a was also achieved with 1.1 equivalents of PIDA in CH3CN–H2O (entry 6). The transformation of 2a into 6a resulted in the cleavage of the C(1)–C(2) bond (type A in Figure 1) followed by C–O bond formation. However, 8-membered biphenyl product (type B), which would be produced by C(1)–C(4) bond cleavage, was not observed. Oxidative β-cleavage reaction of fused cyclobutanols usually gave medium-sized ring products by breaking the transannular bond (type B). To the best of our knowledge, this is the first case of type A regioselectivity in the oxidative β-cleavage of fused cyclobutanols.
Table 1. Optimization of the reaction conditions of PIDA-oxidation of 2a

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>% yield of 6a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.0</td>
<td>HFIP</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>2.0</td>
<td>HFIP</td>
<td>0.2</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>1.1</td>
<td>HFIP</td>
<td>1</td>
<td>66</td>
</tr>
<tr>
<td>4</td>
<td>2.0</td>
<td>CH₂Cl₂</td>
<td>1</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>2.0</td>
<td>CH₃CN</td>
<td>1</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>1.1</td>
<td>CH₃CN</td>
<td>1</td>
<td>83</td>
</tr>
</tbody>
</table>

\(^a\)All reactions were carried out using 0.10 mmol scale of 2a (0.10 M). \(^b\)Isolated yield.

\(^c\)PIDA was added portionwise over 15 min.

With the optimized conditions (entry 5 in Table 1) in hand, we then examined the substrate scope of the diareno-fused bicyclo[4.2.0]octanols (Table 2). Compounds 2b-c and 2d, which have electron-withdrawing and -donating groups on the aromatic ring, respectively, afforded desired phenanthrene-fused dihydrofurans 6b–d in moderate to high yields (entries 1–3). Substrates bearing heteroaromatic or π-extended rings were applicable to this transformation to furnish dihydrofurans 6e and 6f in high yields (entries 4 and 5). Spirocyclic product 6g was also obtained in high yield from 2g (entry 6). In contrast, monomethyl substrate 2h gave a complex mixture of unidentified products (entry 7).
Table 2. Substrate scope of the reaction of 2 with PIDA\textsuperscript{a,b}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrates</th>
<th>Products</th>
<th>%yield of 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(2b) ((R^1 = \text{Cl}), (R^2 = \text{H}))</td>
<td>(6b)</td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>(2c) ((R^1 = \text{H}), (R^2 = \text{Cl}))</td>
<td>(6c)</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>(2d) ((R^1 = \text{MeO}), (R^2 = \text{H}))</td>
<td>(6d)</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>(2e)</td>
<td>(6e)</td>
<td>99</td>
</tr>
<tr>
<td>5</td>
<td>(2f)</td>
<td>(6f)</td>
<td>59</td>
</tr>
<tr>
<td>6</td>
<td>(2g)</td>
<td>(6g)</td>
<td>97</td>
</tr>
<tr>
<td>7</td>
<td>(2h)</td>
<td>(6h)</td>
<td>complex mixture</td>
</tr>
</tbody>
</table>

\textsuperscript{a}All reactions were carried out using 0.10 mmol of 2 (0.10 M). PIDA (1.1 equiv.), CH\textsubscript{3}CN/H\textsubscript{2}O (9:1 v/v), rt. \textsuperscript{b}Isolated yield.

Next, we investigated oxidative \(\beta\)-cleavage using hypochlorous acid (HClO), which Singleton’s group employed in the radical mediated oxidative cleavage of monocyclic cyclobutanol.\textsuperscript{10g} Treating 2a with 4 equivalents of NaOCl·5H\textsubscript{2}O and AcOH, which produced HClO \textit{in situ} in CH\textsubscript{2}Cl\textsubscript{2} at 0 \(^\circ\)C, gave chlorinated compound 7a in 41% yield (Table 3, entry 1). The structure of 7a was determined by X-ray crystallographic analysis. Increasing the reaction temperature of the HClO-oxidation of 2a improved the yield of 7a up to 81% yield (entries 2 and 3). The reaction with a stoichiometric amount of the oxidant resulted in a poor yield of 7a (entry 4). Solvent screening revealed that toluene and CH\textsubscript{3}CN gave lower yields of 7a (entries
5 and 6). 7a should be formed by the β-cleavage of the cyclobutane ring of 2a followed by further chlorinative dearomatization (oxidation)\textsuperscript{12} of \textit{in situ} generated 6a. In fact, when oxidation of 6a was conducted under the same conditions as entry 3, 7a was obtained in 66% yield.

**Table 3. Optimization of the reaction conditions to hemiacetal 7a\textsuperscript{a,b}**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>% yield of 7a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>0</td>
<td>41</td>
</tr>
<tr>
<td>2</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>rt</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>40</td>
<td>81</td>
</tr>
<tr>
<td>4\textsuperscript{c}</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>40</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>toluene</td>
<td>40</td>
<td>17</td>
</tr>
<tr>
<td>6</td>
<td>CH\textsubscript{3}CN</td>
<td>40</td>
<td>43</td>
</tr>
</tbody>
</table>

\textsuperscript{a}All reactions were carried out using 0.20 mmol of 2a (0.10 M). \textsuperscript{b}Isolated yield. \textsuperscript{c}NaOCl∙5H\textsubscript{2}O (1.0 equiv.) and AcOH (1.0 equiv.) were used.

Under the optimal conditions (Table 3, entry 3), the HClO-oxidation of various \textit{tert}-cyclobutanols 2 was conducted (Table 4). Compounds 2b, 2c and 2f respectively afforded hemiacetals 7b, 7c, and 7f in good yields (entries 1, 2, and 5). In contrast, the reactions of compounds 2d and 2e, which have an electron-rich aromatic ring, gave a complex mixture of unidentified products (entries 3 and 4). We speculated that the different reaction scope using HClO from using PIDA might be caused by the reaction mechanism difference in the bond-cleavage. Spirocyclic product 7g was also obtained in high yield from 2g (entry 6). The reaction of monomethyl substrate 2h with HClO, followed by acetylation, afforded keto-acetate 8h in
67% yield as a 1 : 0.17 diastereomer mixture (entry 7). It was difficult to isolate 7h itself, because 7h exists as a mixture of the acetal form and a ring-opened keto-alcohol tautomer in a solution.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrates</th>
<th>Products</th>
<th>% yield of 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2b (R\textsuperscript{1} = Cl, R\textsuperscript{2} = H)</td>
<td>7b</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>2c (R\textsuperscript{1} = H, R\textsuperscript{2} = Cl)</td>
<td>7c</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>2d (R\textsuperscript{1} = MeO, R\textsuperscript{2} = H)</td>
<td>7d</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>2e</td>
<td>7e</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>2f</td>
<td>7f</td>
<td>64</td>
</tr>
<tr>
<td>6\textsuperscript{c}</td>
<td>2g</td>
<td>7g</td>
<td>53</td>
</tr>
<tr>
<td>7\textsuperscript{d}</td>
<td>2h</td>
<td>8h (dr = 1 : 0.17)</td>
<td>67</td>
</tr>
</tbody>
</table>

\textsuperscript{a}All reactions were carried out on a 0.10 mmol scale (0.050 M). NaOCl·5H\textsubscript{2}O (4.0 equiv.), AcOH (4.0 equiv.), CH\textsubscript{2}Cl\textsubscript{2}, 40 °C. \textsuperscript{b}Isolated yield. \textsuperscript{c}NaOCl·5H\textsubscript{2}O (10 equiv.), AcOH (10 equiv.). \textsuperscript{d}After the oxidation of 2h with NaOCl·5H\textsubscript{2}O/AcOH (8.0 equiv.), acetylation of the crude mixture of 7h with Ac\textsubscript{2}O (3.0 equiv.) and DMAP (10 mol%) was carried out at ambient temperature for 16 h.

Previously, it was reported that oxidative β-cleavage of cyclobutanols usually gives acyclic γ-functionalized ketones, which are formed by the addition of an external nucleophile to the ring-opening intermediate.\textsuperscript{9} In contrast, oxidation of 2 afforded 6 or 7 with a hydrofuran ring. We speculated that the
The furan ring was formed by intramolecular addition of the oxygen atom derived from the hydroxy group of 2 prior to an intermolecular trap by an external reagent. This hypothesis was also supported by the following control experiments. In the presence of MeOH (20 equiv.) as an external nucleophile, neither compound 8a nor 9a, which could be formed by the electrophilic addition of MeOH, were detected in the oxidation of 2a with PIDA or NaOCl·5H₂O/AcOH, respectively (Scheme 2).

Scheme 3 summarizes a plausible mechanism. First, the reaction of cyclobutanol 2 with PIDA or HClO, which is generated from NaOCl·5H₂O/AcOH, gives intermediate 10. Then cleavage of the C(1)–C(2) bond selectively occurs to provide tertiary-cationic intermediate 11. This cleavage is driven by the release of the cyclobutane ring strain. The formation of benzyl-cationic intermediate 12 by the cleavage of C(1)–C(4) bond is unfavorable due to the strain of the sp²-rich 8-membered ring. Keto-type intermediate 11 readily tautomerizes into phenol intermediate 13 followed by an intramolecular attack on the tertiary cation to give dihydrofuran 6. The higher nucleophilicity of the phenolic hydroxy group of 13 than that of the carbonyl oxygen of 11 is the rationale for the formation of the furan ring. In the reaction using HClO, phenanthrofuran 6 was further chlorinated to give 7.

**Scheme 2.** Oxidative reactions of 2a in the presence of MeOH.
Conclusions

We demonstrate that oxidative β-cleavage of dibenzo-fused bicyclo[4.2.0]octanols by PIDA gives dihydrophenanthro[9,10-b]furans in an unusual regioselective manner. We also show that oxidation of the alcohols by NaClO/AcOH affords higher oxidized products. This method provides various furan-fused polyaromatic compounds in good yields. These oxidative transformations should serve as a new way to prepare functionalized polycyclic aromatic compounds.

Experimental Section

General Information. For reactions that require heating, oil bath was used as a heat source. Column chromatography was performed on Kanto Kagaku Silica Gel 60 N (spherical, neutral) 100-210 μm. Reactions and chromatography fractions were analyzed by thin-layer chromatography (TLC) carried out on Wako Silicagel 70 F254 TLC Plate-Wako with visualization by ultraviolet (UV) irradiation at 254 nm, phosphomolybdic acid, anisaldehyde, ninhydrin, and/or potassium permanganate staining. NMR was
recorded on a JEOL JNM-LA (500 MHz for $^1$H and 126 MHz for $^{13}$C {$^1$H}) or a JEOL JNM ECZ600R (600 MHz for $^1$H and 151 MHz for $^{13}$C {$^1$H}) and measured in CDCl$_3$ unless otherwise mentioned. Chemical shifts and coupling constants are presented in ppm $\delta$ relative to tetramethylsilane (0.0 ppm) or C$_6$D$_5$H (7.16 ppm) and Hz, respectively. Chloroform-$d_1$ (δ 77.0 ppm) was used as an internal standard for $^{13}$C {$^1$H} NMR. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. IR spectra were recorded on a Shimadzu IRAffinity-1 and the wave numbers of maximum absorption peaks of them are presented in cm$^{-1}$. High-resolution mass spectra (HRMS) were recorded on a JEOL MS700 spectrometer (FAB) or a SHIMADZU LCMS-IT-TOF fitted with an ESI. Melting points were determined on YANACO micro melting point apparatus. X-ray single crystal diffraction analyses were performed on a Rigaku XtaLAB P200 apparatus. All reagents were purchased from chemical companies and used as received. Dehydrated solvents were purchased for the reactions and used without further desiccation unless otherwise mentioned.

Preparation of Substrates 2. Synthesis of substrates 2 was carried out in accordance with the reported procedure.$^5$ Compound 2h was known.$^5$

(2aR*,10bR*)-2,2-Dimethyl-1,10b-dihydrocyclobuta[l]phenanthren-2a(2H)-ol (2a). White solids, Mp. 122–124 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ 8.02 (dd, $J = 8.0$, 1.0 Hz, 1H), 7.95 (d, $J = 8.0$ Hz, 1H), 7.46 (dd, $J = 7.4$, 1.7 Hz, 1H), 7.40 (ddd, $J = 7.4$, 7.4, 1.7 Hz, 1H), 7.36 (ddd, $J = 7.4$, 7.4, 1.5 Hz, 1H), 7.29 (ddd, $J = 7.6$, 7.6, 1.5 Hz, 1H), 7.24 (ddd, $J = 7.4$, 7.4, 1.1 Hz, 1H), 7.15 (dd, $J = 7.2$, 1.1 Hz, 1H), 3.72 (dd, $J = 9.7$, 9.7 Hz, 1H), 2.14 (brs, 1H), 2.05 (dd, $J = 10.3$, 9.7 Hz, 1H), 1.47 (s, 3H), 1.19 (dd, $J = 10.3$, 9.7 Hz, 1H), 0.84 (s, 3H); $^{13}$C {$^1$H} NMR (126 MHz, CDCl$_3$) δ 136.5, 135.8, 132.3, 130.6, 130.1, 128.3, 128.2, 127.9, 127.6, 126.8, 123.4, 122.6, 74.1, 45.7, 43.8, 38.6, 26.8, 24.2; IR (neat) 3406, 2963, 752, cm$^{-1}$; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for C$_{18}$H$_{18}$ONa 273.1250; Found 273.1247.

(2aR*,10bR*)-4-Chloro-2,2-dimethyl-1,10b-dihydrocyclobuta[l]phenanthren-2a(2H)-ol (2b). Colorless oil, $^1$H NMR (500 MHz, CDCl$_3$) δ 7.90 (d, $J = 8.6$ Hz, 1H), 7.84 (d, $J = 7.2$ Hz, 1H), 7.41 (d, $J = 2.3$ Hz, 1H), 7.32 (dd, $J = 8.6$, 2.3 Hz, 1H), 7.27 (td, $J = 7.2$, 1.4 Hz, 1H), 7.23 (td, $J = 7.2$, 1.4 Hz, 1H),...
7.11 (dd, J = 7.2, 1.1 Hz, 1H), 3.65 (dd, J = 9.6, 9.5 Hz, 1H), 2.25 (brs, 1H), 2.05 (dd, J = 10.7, 9.6 Hz, 1H), 1.42 (s, 3H), 1.17 (dd, J = 10.7, 9.6 Hz, 1H), 0.83 (s, 3H); \(^{13}\)C \(^{1}H\) NMR (126 MHz, CDCl\(_3\)) \(\delta\) 137.5, 136.3, 133.1, 130.9, 129.8, 129.7, 128.33, 128.28, 128.2, 126.9, 124.1, 123.3, 74.0, 45.6, 43.7, 38.7, 26.6, 24.1; IR (neat) 3390, 2967, 1447, 764 cm\(^{-1}\); HRMS (FAB) \(m/z\): [M + Na\(^{+}\)] Calcd for C\(_{18}\)H\(_{12}\)ClONa 307.0866; Found 307.0871.

\(2aR^*,10bR^*\)-9-Chloro-2,2-dimethyl-1,10b-dihydrocyclobuta[l]phenanthren-2a(2H)-ol \((2c)\). Colorless oil; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.95 (dd, J = 7.5, 2.0 Hz, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.47-7.45 (m, 1H), 7.40 (td, J = 7.2, 2.0 Hz, 1H), 7.37 (td, J = 7.2, 1.7 Hz, 1H), 7.24 (dd, J = 8.6, 2.3 Hz, 1H), 7.14 (d, J = 2.3 Hz, 1H), 3.67 (dd, J = 10.0, 9.5 Hz, 1H), 2.14 (brs, 1H), 2.06 (dd, J = 10.0, 10.0 Hz, 1H), 1.46 (s, 3H), 1.18 (dd, J = 10.0, 9.5 Hz, 1H), 0.83 (s, 3H); \(^{13}\)C \(^{1}H\) NMR (126 MHz, CDCl\(_3\)) \(\delta\) 138.3, 135.5, 133.3, 131.2, 130.1, 129.2, 128.2, 127.9, 127.8, 126.8, 124.8, 122.4, 74.0, 45.8, 43.4, 38.4, 26.6, 24.1; IR (neat) 3395, 2963, 1443, 764 cm\(^{-1}\); HRMS (FAB) \(m/z\): [M + Na\(^{+}\)] Calcd for C\(_{18}\)H\(_{12}\)ClONa 307.0866; Found 307.0862.

\(2aR^*,10bR^*\)-4-Methoxy-2,2-dimethyl-1,10b-dihydrocyclobuta[l]phenanthren-2a(2H)-ol \((2d)\). White solids, Mp. 93–95 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.88 (d, J = 9.7 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.22 (td, J = 7.1, 1.4 Hz, 1H), 7.15 (td, J = 7.3, 1.1 Hz, 1H), 7.07 (dd, J = 7.5, 1.1 Hz, 1H), 6.92–6.89 (m, 2H), 3.80 (s, 3H), 3.62 (dd, J = 9.7, 9.7 Hz, 1H), 2.31 (brs, 1H), 2.01 (dd, J = 10.7, 9.7 Hz, 1H), 1.41 (s, 3H), 1.16 (t, J = 10.7, 9.7 Hz, 1H), 0.83 (s, 3H); \(^{13}\)C \(^{1}H\) NMR (126 MHz, CDCl\(_3\)) \(\delta\) 158.9, 137.4, 135.6, 130.6, 128.1, 126.9, 126.7, 125.3, 124.0, 122.7, 114.9, 113.8, 74.3, 55.3, 45.5, 43.7, 38.5, 26.9, 24.2; IR (neat) 3410, 2959, 1485, 768 cm\(^{-1}\); HRMS (ESI) \(m/z\): [M + Na\(^{+}\)] Calcd for C\(_{19}\)H\(_{20}\)O\(_2\)Na 303.1356; Found 303.1356.

\(7bR^*,9aR^*\)-9,9-Dimethyl-8,9-dihydrocyclobuta[3,4]naptho[2,1-b]thiophen-9a(7bH)-ol \((2e)\). Colorless solids, Mp. 75–77°C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.65 (d, J = 7.7 Hz, 1H), 7.47 (d, J = 5.3 Hz, 1H), 7.42 (d, J = 5.3 Hz, 1H), 7.26 (td, J = 7.5, 1.4 Hz, 1H), 7.19 (td, J = 7.5, 1.4 Hz, 1H), 7.15 (dd, J = 7.5, 1.7Hz, 1H), 3.79 (dd, J = 10.0, 10.0 Hz, 1H), 2.28 (brs, 1H), 2.03 (dd, J = 10.6, 10.0 Hz, 1H), 1.46 (s, 3H), 1.27 (dd, J = 10.6, 10.0 Hz, 1H), 1.07 (s, 3H); \(^{13}\)C \(^{1}H\) NMR (126 MHz, CDCl\(_3\)) \(\delta\) 138.2, 136.3, 135.3,
129.3, 127.6, 127.2, 126.81, 126.78, 123.5, 122.2, 74.1, 46.2, 45.5, 38.1, 26.6, 24.0; IR (neat) 3426, 2963, 748, 718 cm⁻¹; HRMS (ESI) m/z: [M – H₂O + H]⁺ Calcd for C₁₆H₁₅S 239.0889; Found 239.0890.

(2aR*,12bR*)-2,2-Dimethyl-1,12b-dihydrobenzo[c]cyclobuta[a]phenanthren-2a(2H)-ol (2f). White solids, Mp. 114–116 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.64–8.62 (m, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.85–7.83 (m, 1H), 7.72 (d, J = 8.6 Hz, 1H), 7.51–7.47 (m, 3H), 7.46 (dd, J = 10.2, 10.0 Hz, 1H), 2.44 (brs, 1H), 1.88 (dd, J = 10.5, 10.0 Hz, 1H), 1.46 (s, 3H), 1.23 (dd, J = 10.5, 10.2 Hz, 1H), 0.56 (s, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 136.8, 134.1, 133.5, 131.8, 131.1, 129.8, 129.7, 128.8, 128.2, 127.4, 127.3, 127.11, 127.07, 126.3, 125.6, 125.4, 74.9, 46.5, 45.6, 36.3, 26.0, 24.2; IR (neat) 3387, 2967, 745 cm⁻¹; HRMS (ESI) m/z: [M + Na]⁺ Calcd for C₂₂H₂₀ONa 323.1406; Found 323.1408.

(2aR*,10bR*)-2,2a-Dihydro-10bH-spirocyclobuta[1]phenanthrene-1,1'cyclohexan]-10b-ol (2g). White solids, Mp. 120–122 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.01 (dd, J = 7.7, 1.4 Hz, 1H), 7.93 (d, J = 7.7 Hz, 1H), 7.47 (dd, J = 7.7, 1.4 Hz, 1H), 7.38 (td, J = 7.5, 1.7 Hz, 1H), 7.34 (td, J = 7.5, 1.4 Hz, 1H), 7.29 (td, J = 7.7, 1.4 Hz, 1H), 7.24 (td, J = 7.2, 1.4 Hz, 1H), 7.14 (dd, J = 7.5, 1.7 Hz, 1H), 3.66 (dd, J = 10.3, 9.5 Hz, 1H), 2.31 (dd, J = 10.6, 10.3 Hz, 1H), 2.15–2.14 (m, 2H), 1.76–1.71 (m, 2H), 1.59 (m, 1H), 1.52–1.42 (m, 2H), 1.29 (td, J = 12.9, 3.4, 1H), 1.14 (qdd, J = 12.7, 3.4, 3.4 Hz, 1H), 1.14 (dd, J = 10.6, 9.5 Hz, 1H), 1.02 (qdd, J = 12.9, 2.9, 2.9 Hz, 1H), 0.93 (m, 1H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 136.8, 135.4, 132.3, 130.6, 130.1, 128.3, 128.1, 127.9, 127.4, 126.8, 123.4, 122.5, 74.9, 49.9, 43.3, 36.3, 35.5, 31.6, 26.1, 22.7, 22.2; IR (neat) 3368, 2924, 1447, 748 cm⁻¹; HRMS (ESI) m/z: [M + Na]⁺ Calcd for C₂₁H₂₂ONa 313.1563; Found 313.1565.

General Procedure for Oxidative β-Cleavage of 2a–h with PIDA. To a solution of cyclobutanol 2a–h (0.10 mmol) in CH₃CN/H₂O (9:1, 1.0 mL) was added PIDA (0.11 mmol) at ambient temperature under Ar atmosphere, and the resulting solution was stirred for 1 h. After the completion of the reaction, the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes/EtOAc) to give dihydrofuran 6a–h.

2,2-Dimethyl-2,3-dihydrophenanthro[9,10-b]furan (6a). The reaction was conducted according to the
general procedure with cyclobutanol 2a (25.0 mg, 0.10 mmol), and PIDA (64 mg, 0.20 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1) afforded compound 6a (24.5 mg, 97% yield) as white solids. Mp. 121–122 °C; ^1H NMR (500 MHz, CDCl$_3$) δ 8.69 (d, J = 7.7 Hz, 1H), 8.65 (d, J = 8.3 Hz, 1H), 8.09 (dd, J = 7.5, 1.4 Hz, 1H), 7.67–7.57 (m, 4H), 7.51–7.48 (m, 1H), 3.37 (s, 2H), 1.65 (s, 6H); ^13C {^1H} NMR (126 MHz, CDCl$_3$) δ 152.1, 131.2, 130.6, 126.9, 126.6, 126.34, 126.29, 123.23, 123.16, 122.98, 122.96, 122.5, 122.2, 113.3, 87.6, 42.6, 28.8; IR (neat) 2970, 1359, 752 cm$^{-1}$; HRMS (ESI) m/z: [M + H]$^+$ Calcd for C$_{18}$H$_{17}$O 249.1274; Found 249.1264.

Oxidation of 2a with PIDA in a preparative scale: To a solution of cyclobutanol 2a (501 mg, 2.0 mmol) in CH$_3$CN/H$_2$O (9:1, 20 mL) was added PIDA (709 mg, 2.2 mmol) at ambient temperature under Ar atmosphere, and the resulting solution was stirred for 1 h. After the completion of the reaction, the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes/EtOAc: 10 : 1) to afford dihydrofuran 6a (426 mg, 86% yield) as white solids.

10-Chloro-2,2-dimethyl-2,3-dihydropenanthro[9,10-b]furan (6b). The reaction was conducted according to the general procedure with cyclobutanol 2b (28.4 mg, 0.10 mmol), and PIDA (35 mg, 0.11 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1) afforded compound 6b (17.5 mg, 62% yield) as white solids. Mp. 88–90 °C; ^1H NMR (500 MHz, CDCl$_3$) δ 8.58 (d, J = 8.9 Hz, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 2.3 Hz, 1H), 7.61–7.59 (m, 2H), 7.57 (dd, J = 8.9, 2.3 Hz, 1H), 7.49 (ddd, J = 8.5, 5.6, 2.9, 1H), 3.36 (s, 2H), 1.64 (s, 6H); ^13C {^1H} NMR (126 MHz, CDCl$_3$) δ 151.1, 132.4, 130.5, 129.5, 127.2, 126.8, 126.2, 124.7, 123.6, 123.4, 123.2, 123.1, 121.6, 114.7, 88.0, 42.6, 28.8; IR (neat) 2970, 752 cm$^{-1}$; HRMS (FAB) m/z: [M + H]$^+$ Calcd for C$_{18}$H$_{16}$ClO 283.0890; Found 283.0892.

5-Chloro-2,2-dimethyl-2,3-dihydropenanthro[9,10-b]furan (6c). The reaction was conducted according to the general procedure with cyclobutanol 2c (28.4 mg, 0.10 mmol), and PIDA (35 mg, 0.11 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1) afforded compound 6c (22.8 mg, 81% yield) as white solids. Mp. 99–101 °C; ^1H NMR (600 MHz, CDCl$_3$) δ 8.59 (d, J = 7.6 Hz, 1H), 8.53 (d, J = 9.0 Hz, 1H), 8.08 (d, J = 7.6 Hz, 1H), 7.65 (ddd, J = 8.3, 6.9, 1.4 Hz, 1H), 7.62 (dd, J = 7.6, 6.9 Hz, 1H), 7.56 (d, J = 2.1 Hz, 1H), 7.41 (dd, J = 9.0, 2.1 Hz, 1H), 3.32 (s, 2H), 1.64 (s, 6H); ^13C
{^1}H NMR (151 MHz, CDCl\textsubscript{3}) \(\delta\) 153.1, 132.9, 131.8, 130.8, 126.8, 126.5, 124.9, 124.8, 123.4, 122.9, 122.4, 122.3, 122.1, 112.5, 88.0, 42.4, 28.7; IR (neat) 764 cm\(^{-1}\); HRMS (ESI) \(m/z\): [M + H]\(^+\) Calcd for C\textsubscript{18}H\textsubscript{16}ClO 283.0884; Found 283.0882.

10-Methoxy-2,2-dimethyl-2,3-dihydropyrido[9,10-b]furan (6d). The reaction was conducted according to the general procedure with cyclobutanol 2d (28.0 mg, 0.10 mmol), and PIDA (35 mg, 0.11 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1) afforded compound 6d (25.3 mg, 91% yield) as white solids.

Mp. 121–122 °C; ^1H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.57 (d, \(J = 9.2\) Hz, 1H), 8.55 (d, \(J = 8.3\) Hz, 1H), 7.59 (dd, \(J = 7.9, 1.0\) Hz, 1H), 7.52 (ddd, \(J = 8.0, 6.9, 1.2\) Hz, 1H), 7.47 (ddd, \(J = 8.3, 6.9, 1.4\) Hz, 1H), 7.42 (d, \(J = 2.9\) Hz, 1H), 7.26 (dd, \(J = 9.2, 2.9\) Hz, 1H), 4.00 (s, 3H), 3.37 (s, 2H), 1.65 (s, 6H); ^13C \{^1\}H NMR (126 MHz, CDCl\textsubscript{3}) \(\delta\) 158.3, 151.7, 129.4, 126.8, 125.9, 125.5, 124.7, 123.6, 123.3, 122.9, 122.7, 117.2, 113.8, 102.0, 87.5, 55.5, 42.7, 28.8; IR (neat) 2966, 752 cm\(^{-1}\); HRMS (FAB) \(m/z\): [M + H]\(^+\) Calcd for C\textsubscript{19}H\textsubscript{19}O\textsubscript{2} 279.1385; Found 279.1380.

2,2-Dimethyl-2,3-dihydrothieno[2',3':3,4]naptho[2,1-b]furan (6e). The reaction was conducted according to the general procedure with cyclobutanol 2e (25.6 mg, 0.10 mmol), and PIDA (35 mg, 0.11 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1) afforded compound 6e (25.2 mg, 99% yield) as white solids.

Mp. 127–128 °C; ^1H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.32 (d, \(J = 8.3\) Hz, 1H), 8.00 (d, \(J = 5.2\) Hz, 1H), 7.65 (d, \(J = 8.0\) Hz, 1H), 7.55 (d, \(J = 5.4\) Hz, 1H), 7.52 (ddd, \(J = 6.9, 1.2\) Hz, 1H), 7.45 (ddd, \(J = 8.3, 6.9, 1.2\) Hz, 1H), 3.39 (s, 2H), 1.66 (s, 6H); ^13C \{^1\}H NMR (126 MHz, CDCl\textsubscript{3}) \(\delta\) 150.6, 138.1, 129.6, 125.8, 125.4, 125.2, 124.3, 123.6, 123.2, 122.9, 122.5, 113.5, 89.2, 42.3, 28.7; IR (neat) 2970, 756 cm\(^{-1}\); HRMS (ESI) \(m/z\): [M + H]\(^+\) Calcd for C\textsubscript{16}H\textsubscript{15}O\textsubscript{2} 255.0838; Found 255.0839.

2,2-Dimethyl-1,2-dihydrobenzo[3,4]phenanthro[1,2-b]furan (6f). The reaction was conducted according to the general procedure with cyclobutanol 2f (30.0 mg, 0.10 mmol), and PIDA (35 mg, 0.11 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1) afforded compound 6f (17.6 mg, 59% yield) as a yellowish oil.

^1H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 9.10 (dd, \(J = 8.6, 8.3\) Hz, 2H), 8.09 (d, \(J = 8.6\) Hz, 1H), 8.02 (d, \(J = 8.0\) Hz, 1H), 7.92 (d, \(J = 8.6\) Hz, 1H), 7.72(d, \(J = 7.7\) Hz, 1H), 7.67 (t, \(J = 7.7\) Hz, 1H), 7.63–7.59 (m, 2H), 7.53–7.50 (m, 1H), 3.44 (s, 2H), 1.67 (s, 6H); ^13C \{^1\}H NMR (126 MHz,
CDCl$_3$ $\delta$ 152.7, 137.5, 133.4, 131.4, 130.4, 128.8, 128.7, 128.3, 128.1, 127.3, 126.5, 126.3, 126.0, 125.7, 123.0, 122.7, 120.6, 120.2, 114.9, 87.9, 42.6, 28.8; IR (neat) 2970, 760 cm$^{-1}$; HRMS (ESI) $m/z$: [M + H]$^+$ Calcd for C$_{22}$H$_{19}$O 299.1430; Found 299.1429.

3'H-Spiro[cyclohexane-1,2'-phenanthro[9,10-b]furan] (6g). The reaction was conducted according to the general procedure with cyclobutanol 2g (29.0 mg, 0.10 mmol), and PIDA (35 mg, 0.11 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1) afforded compound 6g (28.0 mg, 97% yield) as colorless solids. Mp. 128–129 °C; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.69 (dd, $J = 7.3, 2.1$ Hz, 1H), 8.66 (d, $J = 8.3$ Hz, 1H), 8.16–8.13 (m, 1H), 7.66 (td, $J = 6.9, 1.7$ Hz, 1H), 7.65–7.62 (m, 2H), 7.60 (td, $J = 6.9, 1.2$ Hz, 1H), 7.50 (ddd, $J = 9.2, 8.3, 1.6$ Hz, 1H), 3.31 (s, 2H), 2.05–2.01 (m, 2H), 1.98–1.92 (m, 2H), 1.84–1.79 (m, 2H), 1.65–1.53 (m, 4H); $^{13}$C {$^1$H} NMR (126 MHz, CDCl$_3$) $\delta$ 152.1, 131.2, 130.7, 126.9, 126.5, 126.3, 126.2, 123.2, 123.0, 122.93, 122.86, 122.6, 122.2, 113.0, 89.5, 40.9, 37.6, 25.3, 23.1; IR (neat) 2931, 752 cm$^{-1}$; HRMS (FAB) $m/z$: [M + H]$^+$ Calcd for C$_{21}$H$_{21}$O 289.1592; Found 289.1598.

**General Procedure for Oxidative β-Cleavage of 2a–g with NaOCl-5H$_2$O/AcOH.** To a solution of cyclobutanol 2a–g (0.10 mmol) and NaOCl-5H$_2$O (0.40 mmol) in CH$_2$Cl$_2$ (2.0 mL) was added AcOH (0.40 mmol) at 40 °C under Ar atmosphere and the resulting solution was stirred for 1 h. After the completion of the reaction, the reaction mixture was quenched with sat. Na$_2$SO$_3$ aq. and extracted with EtOAc three times. The combined organic layers were washed with sat. NaHCO$_3$ aq. and brine, dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified with silica gel column chromatography (hexanes/EtOAc) to give hemiacetal 7a–g.

(3aS*,11bS*)-3a-chloro-2,2-dimethyl-3,3a-dihydropheanthro[9,10-b]furan-11b(2H)-ol (7a). The reaction was conducted according to the general procedure with cyclobutanol 2a (25.0 mg, 0.10 mmol), NaOCl-5H$_2$O (132 mg, 0.40 mmol) and AcOH (46 μL, 0.40 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1 to 3:1) afforded compound 7a (24.4 mg, 81% yield) as white solids. Mp. 113–115 °C; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.00 (dd, 1H, $J = 7.7, 1.7$ Hz), 7.92 (dd, 1H, $J = 7.2, 2.0$ Hz), 7.88 (dd, 1H, $J = 7.7, 0.9$ Hz), 7.74 (dd, 1H, $J = 7.4, 1.7$ Hz), 7.48 (td, 1H, $J = 7.7, 1.4$ Hz), 7.38–7.46 (m, 3H), 3.42 (brs, 1H), 2.99 (s, 2H), 1.57 (s, 3H), 0.76 (s, 3H); $^1$H NMR (500 MHz,C$_6$D$_6$) $\delta$ 8.06-8.08 (m, 2H).
1H), 7.54–7.57 (m, 1H), 7.50–7.53 (m, 2H), 7.11–7.14 (m, 2H), 7.02–7.08 (m, 2H), 3.20 (s, 1H), 2.82 (d, \( J = 12.9 \) Hz, 1H), 2.64 (d, \( J = 12.9 \) Hz, 1H), 1.47 (s, 3H), 0.65 (s, 3H); \(^{13}\)C \(^1\)H NMR (126 MHz, CDCl\(_3\)) \( \delta \) 135.7, 133.7, 131.3, 130.7, 129.8, 129.1, 128.6, 128.5, 128.3, 127.0, 124.0, 123.8, 101.9, 80.7, 74.5, 51.3, 31.2, 28.2; IR (neat) 3502, 2974, 756, 732 cm\(^{-1}\); HRMS (ESI) \textit{m/z}: [M + Na]\(^+\) Calcd for C\(_{18}\)H\(_{17}\)ClO\(_2\)Na 323.0809; Found 323.0808.

X-ray crystallographic analysis (CCDC 2103959): Recrystallization from pentane/MeOH gave colorless platelets suitable for X-ray crystal structural analysis: orthorhombic \( P2_12_12_1 \); \( a = 10.3098(3), b = 11.4153(3), c = 12.3089(20) \); \( V = 1448.63(6) \), \( Z = 4 \), \( D_\text{x} = 1.379 \).

**Oxidation of 2a with NaOCl\(\cdot\)5H\(_2\)O/AcOH in a preparative scale:** To a solution of cyclobutanol 2a (501 mg, 2.0 mmol) and NaOCl\(\cdot\)5H\(_2\)O (2.64 g, 16 mmol) in CH\(_2\)Cl\(_2\) (40 mL) was added AcOH (1.0 mL, 16 mmol) at 40 °C under Ar atmosphere and the resulting solution was stirred for 1 h. After the completion of the reaction, the reaction mixture was quenched with sat. Na\(_2\)S\(_2\)O\(_3\) aq. and extracted with EtOAc three times. The combined organic layers were washed with sat. NaHCO\(_3\) aq. and brine, dried over Na\(_2\)SO\(_4\), filtered, and concentrated \textit{in vacuo}. The residue was purified with silica gel column chromatography (hexanes/EtOAc: 10 : 1 to 3 : 1) to afford hemiacetal 7a (434 mg, 72% yield) as white solids.

\((3aS^*,11bS^*)\)-3a,10-Dichloro-2,2-dimethyl-3,3a-dihydrophenanthro[9,10-b]furan-11b(2H)-ol (7b). The reaction was conducted according to the general procedure with cyclobutanol 2b (28.4 mg, 0.10 mmol), NaOCl\(\cdot\)5H\(_2\)O (132 mg, 0.40 mmol) and AcOH (46 \( \mu \)L, 0.40 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1 to 3:1) afforded compound 7b (21.1 mg, 63% yield) as white solids. Mp. 114–116 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 8.01 (d, \( J = 2.1 \) Hz, 1H), 7.88–7.87 (m, 1H), 7.91 (d, \( J = 9.0 \) Hz, 1H), 7.73–7.72 (m, 1H), 7.46–7.42 (m, 3H), 3.43 (s, -OH), 3.03 (d, \( J = 13.1 \) Hz, 1H), 2.99 (d, \( J = 13.1 \) Hz, 1H), 1.56 (s, 3H), 0.78 (s, 3H); \(^{13}\)C \(^1\)H NMR (126 MHz, CDCl\(_3\)) \( \delta \) 135.8, 135.5, 134.6, 129.90, 129.86, 129.81, 129.3, 128.8, 128.4, 127.4, 125.3, 123.9, 101.4, 81.2, 74.5, 51.2, 31.2, 28.1; IR (neat): 3541, 2974, 1477, 764, 729 cm\(^{-1}\); HRMS (ESI) \textit{m/z}: [M + Na]\(^+\) Calcd for C\(_{18}\)H\(_{16}\)ClO\(_2\)Na 357.0420; Found 357.0438.

\((3aS^*,11bS^*)\)-3a,5-Dichloro-2,2-dimethyl-3,3a-dihydrophenanthro[9,10-b]furan-11b(2H)-ol (7c). The reaction was conducted according to the general procedure with cyclobutanol 2c (28.4 mg, 0.10 mmol),
NaOCl-5H_2O (132 mg, 0.40 mmol) and AcOH (46 μL, 0.40 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1 to 3:1) afforded compound 7c (24.8 mg, 74% yield) as white solids. Mp. 109–111 °C; ^1H NMR (500 MHz, CDCl_3): δ 7.99 (dd, J = 7.4, 1.7 Hz, 1H), 7.86 (d, J = 8.6 Hz, 1H), 7.82 (dd, J = 7.7, 1.1 Hz, 1H), 7.72 (d, J = 2.3 Hz, 1H), 7.49 (td, J = 7.4, 1.7 Hz, 1H), 7.45 (td, J = 7.4, 1.3 Hz, 1H), 7.40 (dd, J = 8.6, 2.3 Hz, 1H), 3.42 (s, 1H), 2.97 (d, J = 13.2 Hz, 1H), 2.89 (d, J = 13.2 Hz, 1H), 1.57 (s, 3H), 0.84 (s, 3H); ^13C (1H) NMR (126 MHz, CDCl_3): δ 137.8, 134.1, 133.6, 129.9, 129.4, 129.3, 129.0, 128.4, 127.2, 125.5, 123.7, 101.8, 80.6, 74.6, 51.5, 31.1, 28.4; IR (neat): 3510, 2974, 764 cm⁻¹; HRMS (ESI) m/z: [M + Na]^+ Calcd for C_{18}H_{16}Cl_2O_2Na 357.0420; Found 357.0422.

(3a'S,11b'S')-13b-Chloro-2,2-dimethyl-1,13b-dihydrobenzo[3,4]phenanthro[1,2-b]furan-3a(2H)-ol (7f). The reaction was conducted according to the general procedure with cyclobutanol 2f (30.0 mg, 0.10 mmol), NaOCl-5H_2O (132 mg, 0.40 mmol) and AcOH (46 μL, 0.40 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1 to 3:1) afforded compound 7f (22.5 mg, 64% yield) as white solids. Mp. 114–116 °C; ^1H NMR (500 MHz, CDCl_3): δ 8.55 (d, J = 8.3 Hz, 1H), 8.39 (d, J = 8.6 Hz, 1H), 8.17 (s, 1H), 7.98–7.95 (m, 1H), 7.89–7.85 (m, 1H), 7.68–7.64 (m, 1H), 7.48 (dd, J = 9.5, 1.7 Hz, 1H), 7.46 (t, J = 6.4 Hz, 1H), 7.44 (dd, J = 9.5, 1.7 Hz, 1H), 3.49 (brs, 1H), 2.94 (s, 2H), 1.59 (s, 3H), 0.68 (s, 3H); ^13C (1H) NMR (126 MHz, CDCl_3): δ 136.0, 132.6, 132.2, 132.0, 130.5, 130.2, 129.8, 128.6, 128.2, 128.1, 128.0, 127.3, 127.0, 126.8, 125.0, 124.5, 102.3, 80.8, 75.2, 51.2, 31.1, 28.3; IR (neat) 1365, 756 cm⁻¹; HRMS (ESI) m/z: [M + K]^+ Calcd for C_{22}H_{19}ClO_2K 389.0705; Found 389.0713.

(3a'S,11b'S')-3a'-Chloro-3,3a'-dihydro-11b'H-spiro[cyclohexane-1,2'-phenanthro[9,10-b]furan-11b'-ol (7g). The reaction was conducted according to the general procedure with cyclobutanol 2g (29.0 mg, mmol), NaOCl-5H_2O (132 mg, 0.40 mmol) and AcOH (46 μL, 0.40 mmol). Purification by silica gel column chromatography (hexanes/EtOAc: 10:1 to 3:1) afforded compound 7g (18.1 mg, 53% yield) as a colorless oil. ^1H NMR (600 MHz, CDCl_3): δ 8.01 (d, J = 7.6 Hz, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 8.3 Hz, 1H), 7.75 (dd, J = 7.6, 1.4 Hz, 1H), 7.48 (td, J = 7.6, 1.4 Hz, 1H), 7.43 (td, J = 8.3, 1.4 Hz, 1H), 7.41–7.38 (m, 2H), 3.48 (brs, 1H), 2.93 (d, J = 13.5 Hz, 1H), 2.85 (d, J = 13.5 Hz, 1H), 1.99–1.93 (m, 1H), 1.90–1.89 (m, 1H), 1.78–1.75 (m, 1H), 1.51–1.48 (m, 1H), 1.40–1.36 (m, 2H), 1.27–1.24 (m, 1H),
1.18–1.15 (m, 1H), 1.07–1.03 (m, 1H), 0.91–0.88 (m, 1H); $^{13}$C \{${^1}$H\} NMR (151 MHz, CDCl$_3$) $\delta$ 136.1, 134.1, 131.2, 130.5, 129.7, 129.1, 128.6, 128.4, 128.2, 127.1, 123.9, 123.6, 101.3, 82.6, 75.7, 49.5, 40.3, 36.7, 25.1, 23.6, 23.5; IR (neat); 3507, 2932, 756, 729 cm$^{-1}$; HRMS (ESI) \textit{m/z}: [M + Na]$^+$ Calcd for C$_{21}$H$_{21}$ClO$_3$Na 363.1122; Found 363.1126.

$(S^*)$-1-\{(S* and R*)-9-chloro-10-oxo-9,10-dihydrophenanthren-9-yl\}propan-2-yl acetate (8h). To a solution of cyclobutanol 2h (49.0 mg, 0.21 mmol) and NaOCl∙5H$_2$O (273 mg, 1.66 mmol) in CH$_2$Cl$_2$ (2.0 mL) was added AcOH (95 $\mu$L, 1.66 mmol) at 40 ºC under Ar atmosphere and the resulting solution was stirred for 30 min. After the completion of the reaction, the reaction mixture was quenched with sat. Na$_2$S$_2$O$_3$ aq. and extracted with EtOAc three times. The combined organic layers were washed with sat. NaHCO$_3$ aq. and brine, dried over Na$_2$SO$_4$, filtered, and concentrated \textit{in vacuo}. And then, the crude was dissolved in CH$_2$Cl$_2$ (2.0 mL) and acetic anhydride (59 $\mu$L, 0.62 mmol) and 4-dimethylaminopyridine (2.6 mg, 0.021 mmol) successively added to the mixture at ambient temperature and the resulting solution was stirred for 16 h. After the completion of the reaction, the reaction mixture was quenched with H$_2$O and brine, then extracted with EtOAc three times. The combined organic layers were washed with sat. NaHCO$_3$ aq. and brine, dried over Na$_2$SO$_4$, filtered, and concentrated \textit{in vacuo}. The residue was purified by silica gel column chromatography (hexane/AcOEt = 10:1 to 3:1) to afford product 8h (45.6 mg, 67% over 2 steps) as colorless solids in a 1 : 0.17 diastereomeric ratio. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.28 (dd, $J$ = 8.0, 1.4 Hz, 0.17H), 8.13 (d, $J$ = 7.7, 1H), 8.06 (d, $J$ = 8.6 Hz, 0.17H), 8.04–8.02 (m, 0.17H), 8.00 (d, $J$ = 8.0 Hz, 1H), 7.98–7.96 (m, 1H), 7.87 (dd, $J$ = 8.6, 8.0, 7.6 Hz, 1H), 7.75–7.69 (m, 1.34H), 7.49–7.43 (m, 3.51H), 4.95 (dqd, $J$ = 8.9, 6.3, 3.2 Hz, 1H), 4.47 (dqd, $J$ = 11.2, 5.7, 2.9 Hz, 0.17H), 3.32 (dd, $J$ = 14.0, 11.2 Hz, 0.17H), 2.85 (dd, $J$ = 14.8, 8.9 Hz, 1H), 2.78 (dd, $J$ = 14.8, 3.2 Hz, 1H), 2.69 (dd, $J$ = 14.0, 2.9 Hz, 0.17H), 1.61 (s, 3H), 1.17 (s, 0.51H), 1.13 (d, $J$ = 5.7 Hz, 0.51H), 1.12 (d, $J$ = 6.3 Hz, 3H); $^{13}$C \{${^1}$H\} NMR (126 MHz, CDCl$_3$, signals from the minor diastereomer are marked with an asterisk) $\delta$ 192.4, 191.9*, 169.9, 169.5*, 137.6, 137.0*, 136.1, 136.0*, 135.2*, 135.1, 129.7*, 129.5, 129.2, 129.14, 129.10, 129.0*, 128.9*, 128.8, 128.7, 128.3, 127.7*, 123.9, 123.7*, 123.3*, 123.2, 69.5, 67.9*, 67.5, 66.1*, 48.9*, 47.3, 20.9, 20.5,
20.2*, 19.9* (three peaks are unidentified.); IR (neat) 1736, 1690, 1450, 1238, 729 cm⁻¹; HRMS (ESI) m/z: [M + Na]⁺ Calcd for C₁₉H₁₇ClO₃Na 351.0758; Found 351.0769.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: xxxxxx.

¹H, ¹³C {¹H} NMR spectra of new compounds and X-ray crystallography (PDF). Crystallographic data for 7a (CCDC 2103959) (CIF).

AUTHOR INFORMATION

Corresponding Author

Kiyosei Takasu — Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyō-ku, Kyoto 606-8501, Japan; orcid.org/0000-0002-1798-7919; Phone: (+81)-75-753-4553; E-mail: kay-t@pharm.kyoto-u.ac.jp; Fax: (+81)-75-753-4604

Authors

Hayate Kinouchi — Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyō-ku, Kyoto 606-8501, Japan

Kazuma Sugimoto — Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyō-ku, Kyoto 606-8501, Japan

Yousuke Yamaoka — Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyō-ku, Kyoto 606-8501, Japan; orcid.org/0000-0003-3641-8823

Hiroshi Takikawa — Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyō-ku, Kyoto 606-8501, Japan;
Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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REFERENCES


