Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Formation of α-Hydroxy-β-diketones via Hydroxylation of Isoxazolium Salts: Stereoselective Approach to Angular *cis*-Diol in Polycyclic System

Hiroshi Takikawa, Akiomi Takada, Katsuyoshi Hilita, and Keisuke Suzuki*

[*] Department of Chemistry, Tokyo Institute of Technology, SORST–JST Agency,
2-12-1 O-okayama, Meguro-ku, Tokyo 152-8551 (Japan)

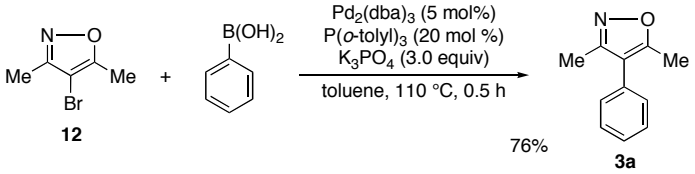
Supporting Information

General methods

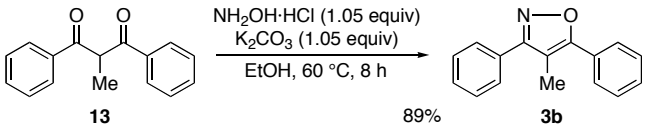
All reactions utilizing air- or moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry argon or nitrogen. Ethereal solvents (anhydrous; Kanto Chemical Co., Inc.) were used as received. CH_2Cl_2 was distilled successively from P_2O_5 and CaH_2, and stored over 4A molecular sieves. Trimethyloxonium tetrafluoroborate was purified according to the literature procedure.[1] Thin layer chromatography (TLC) was performed on Merck precoated plates (silica gel 60 F254, Art 5715, 0.25 mm) and visualized by fluorescence quenching under UV light or by staining with phosphomolybdic acid. Silica-gel preparative thin-layer chromatography (PTLC) was performed using plates prepared from Merck Kieselgel 60 PF 254 (Art 7747). Silica-gel column chromatography was performed on silica gel 60N (spherical, neutral, 23–210 μm) from Kanto chemical. Melting point (mp) determinations were performed using a Yanaco MP-500 instrument and are uncorrected. ^{1}H NMR and ^{13}C NMR were measured on a JEOL JNM Lambda-400 spectrometer and a Bruker DRX-500 spectrometer. Chemical shifts are expressed in parts per million (PPM) downfield from internal standard (tetramethylsilane, 0.00 ppm), and coupling constants are reported as hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared (IR) spectra were recorded on a Perkin-Elmer Spectrum 100 FTIR spectrometer. Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectra were recorded by using a Perkin-Elmer 100 FTIR spectrometer equipped with a universal ATR sampling accessory. Optical rotations ($[\alpha]_D$) were measured on a JASCO DIP-1000 polarimeter. High performance liquid chromatography (HPLC) analyses were performed using a JASCO CO-2060 plus for column thermostat, UV-2075 plus for UV/VIS detector, CD-2095 plus for chiral detector, and PU-2089 plus for HPLC pump. Enantiomeric excesses were assessed by HPLC analysis on a chiral stationary phase, CHIRALPAK® AD-H or CHIRALCEL® OD-H or CHIRALPAK® IA (Daicel Chemical Ind., Ltd., ϕ 0.48 mm x 25 cm). High resolution mass spectra (HRMS) were obtained with a JEOL JMS-700 spectrometer. Recycling preparative HPLC was performed on LC-918 (Japan Analytical Industry Co., Ltd.) equipped with a hydrophobic size exclusion chromatography column, JAIGEL-2H (Japan Analytical Industry Co., Ltd.) or highly purified silica-gel HPLC column, Mightysil Si60 (Kanto Chemical Co., Inc.).

[1] T. J. Curphey, *Org. Synth.* **1971**, *51*, 142–147.

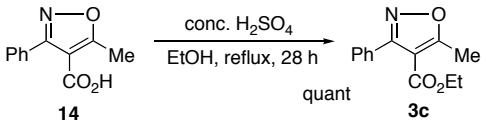
Preparation of isoxazoles 3a–3e



The flame-dried 2-necked flask was placed 4-bromo-3,5-dimethylisoxazole[2] (**12**, 835 mg, 4.56 mmol) in toluene (15 mL) and three freeze-pump-thaw cycles were performed. The flask was charged with $Pd_2(dba)_3$ (134 mg, 0.233 mmol), P(*o*-tolyl)$_3$ (279 mg, 0.917 mmol), K_3PO_4 (2.90 g, 13.7 mmol) and phenylboronic acid (1.14 g, 9.35 mmol) under an argon atmosphere, and the mixture was heated at 110 °C. The reaction mixture was stirred for 0.5 h, and then cooled to room temperature followed by filtration through Celite® pad. The filtrate was washed with water and brine, dried over $MgSO_4$. Concentration of the organic layer under reduced pressure provided the crude product, which was purified by recycling preparative HPLC (column: JAIGEL-1H+2H, eluent: $CHCl_3$) to give 3,5-dimethyl-4-phenylisoxazole (**3a**, 600 mg, 76%) as colorless oil. The spectroscopic data were identical with those reported in the literature.[3]



To a suspension of 1,3-diketone **13**[4] (185 mg, 0.776 mmol) and K_2CO_3 (112 mg, 0.810 mmol) in EtOH (3.9 mL) was added hydroxylamine hydrochloride (56.4 mg, 0.811 mmol) at room temperature. The reaction was heated to 60 °C and stirred for 8 h at this temperature. The mixture was concentrated under reduced pressure. The products were extracted with EtOAc (x3), and the combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was washed with hexane/Et_2O (v/v = 1/2) to afford isoxazole **3b** (163 mg, 89%) as a white solid. The spectroscopic data were identical with those reported in the literature.[5]



To a solution of 5-methyl-3-phenylisoxazole-4-carboxylic acid (**14**, 3.05 g, 15.0 mmol) in EtOH (30 mL) was added conc. H_2SO_4 (5 mL) at room temperature. The reaction was heated under reflux and stirred for 28 h at this temperature. After cooling to room temperature, the reaction was quenched by the slow addition of saturated $NaHCO_3$. The products were extracted with EtOAc (x2), and the combined organic layer was washed

---

[2] T. Sakakibara, T. Kume, T. Hase. *Chemistry Express* **1989**, *4*, 85–88.
[3] a) A. K. Sahoo, T. Oda, Y. Nakao, T. Hiyama, *Adv. Synth. Catal.* **2004**, *346*, 1715–1727; b) Sharada S. L., *Synth. Commun.* **1994**, *24*, 709–720.
[4] C. Wiles, P. Watts, S. J. Haswell, E. Pombo-Villarb, *Tetrahedron Lett.* **2002**, *43*, 2945–2948.
[5] S. Auricchio, O. Vajna De Pava, E. Vera, *Synthesis* **1979**, 116–117.

with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (hexane/EtOAc = 1/4) to give isoxazole **3c** (3.47 g, quant) as colorless, sticky oil.

R_f 0.6 (hexane/EtOAc = 2/1);

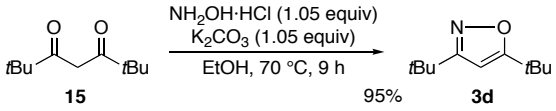
mp 43.0–47.0 ºC [crystallization at 5 °C, colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, 3H, *J* = 7.1 Hz), 2.74 (s, 3H), 4.24 (q, 2H, *J* = 7.1 Hz), 7.41–7.49 (m, 3H), 7.61–7.64 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 13.8, 60.5, 108.3, 127.7, 128.4, 129.2, 129.5, 161.7, 162.3, 175.6;

IR (ATR) 3667, 3418, 2984, 1960, 1890, 1716, 1603, 1447, 1309, 1138, 1100 cm^{-1};

Anal. Calc'd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06; Found: C, 67.29; H, 5.66; N, 5.87.



To a suspension of 1,3-diketone **15** (1.93 g, 10.5 mmol) and K_2CO_3 (1.51 g, 10.9 mmol) in EtOH (17 mL) was added hydroxylamine hydrochloride (763 mg, 11.0 mmol) at room temperature. The reaction was heated to 70 °C and stirred for 9 h at this temperature. The mixture was concentrated under reduced pressure. The products were extracted with EtOAc (x3), and the combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford analytically pure isoxazole **3d** (1.81 g, 95%) as a white solid.

R_f 0.45 (hexane/EtOAc = 9/1);

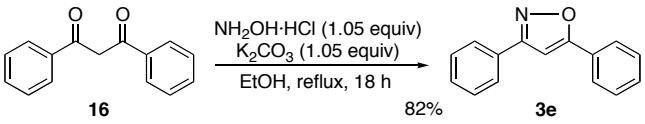
Sublimation point 80.0–83.0 ºC [hexane, colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 1.33 (s, 9H), 5.80 (s, 1H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 29.5, 31.9, 32.6, 95.8, 171.7, 180.6;

IR (ATR) 2964, 1593, 1466, 1406, 1366, 1253 cm^{-1};

Anal. Calc'd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73; Found: C, 72.66; H, 10.80; N, 7.61.



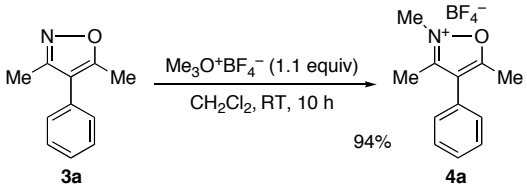
To a suspension of 1,3-diketone **16** (6.73 g, 30.0 mmol) and K_2CO_3 (4.35 g, 31.5 mmol) in EtOH (50 mL) was added hydroxylamine hydrochloride (2.19 g, 31.5 mmol) at room temperature. The reaction was heated under reflux and stirred for 18 h at this temperature. The mixture was concentrated under reduced pressure. The products were extracted with EtOAc (x3), and the combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was washed with EtOH to afford isoxazole **3e** (5.22 g, 82 %) as a white solid. The spectroscopic data were identical with those reported in the literature.[6]

---

[6] a) L. Cecchi, F. D. Sarlo, F. Machetti, *Eur. J. Org. Chem.* **2006**, 4852–4860; b) T. V. Hansen, P. Wu, V. V. Fokin, *J.*

General procedure for the preparation of isoxazolium salts

(Scheme 2)



3a **4a**

The preparation of isoxazolium salt **4a** is representative. To a solution of isoxazole **3a** (745 mg, 4.30 mmol) in CH_2Cl_2 (8.6 mL), trimethyloxonium tetrafluoroborate (90%, 777 mg, 4.7 mmol) was added at 0 °C, and the mixture was allowed to warm to room temperature. After stirring for 10 h, MeOH was added to the mixture and the solvents were evaporated under reduced pressure. The residue was triturated with Et_2O followed by filtration to give isoxazolium salt **4a** (1.11 g, 94%).

mp 94.5–95.0 ºC [acetone/Et_2O (vapor diffusion), colorless needles];

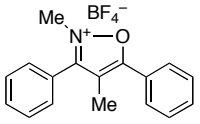
^{1}H NMR (400 MHz, acetone-d_6) δ 2.68 (s, 3H), 2.70 (s, 3H), 4.44 (s, 3H), 7.52–7.62 (m, 5H);

^{13}C NMR (100 MHz, acetone-d_6) δ 11.46, 11.48, 38.8, 122.1, 126.7, 130.1, 130.46, 130.51, 159.7, 169.8;

IR (ATR) 3056, 1621, 1557, 1496, 1424, 1253, 1026, 783, 713 cm^{-1};

Anal. Calc'd for $C_{12}H_{14}BF_4NO$: C, 52.40; H, 5.13; N, 5.09; Found: C, 52.41; H, 5.39; N, 5.12.

(Table 1, entry 1)



4b

Prepared according to the general procedure from isoxazole **3b** (607 mg, 2.58 mmol) and trimethyloxonium tetrafluoroborate (90%, 437 mg, 2.7 mmol) under the conditions indicated in Table 1. The crude product was purified by trituration with Et_2O to give isoxazolium salt **4b** (849 mg, 97%) as a colorless solid.

mp 188.5–190.0 ºC [acetone/hexane (vapor diffusion), colorless needles];

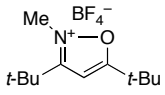
^{1}H NMR (400 MHz, acetone-d_6) δ 2.42 (s, 3H), 4.48 (s, 3H), 7.70–7.85 (m, 6H), 7.87–7.90 (m, 2H), 8.01–8.04 (m, 2H);

^{13}C NMR (100 MHz, acetone-d_6) δ 9.0, 40.0, 116.0, 123.4, 125.0, 129.2, 130.5, 130.6, 130.7, 133.8, 133.9, 161.2, 168.2;

IR (ATR) 3063, 1612, 1470, 1430, 1095, 1049, 1035 cm^{-1};

Anal. Calc'd for $C_{17}H_{16}BF_4NO$: C, 60.57; H, 4.78; N, 4.15; Found: C, 60.56; H, 4.73; N, 4.07.

(Table 1, entry 3)



4d

Prepared according to the general procedure from isoxazole **3d** (777 mg, 4.29 mmol) and trimethyloxonium tetrafluoroborate (90%, 741 mg, 4.5 mmol) under the conditions indicated in Table 1. The crude product was purified by trituration with Et_2O to give isoxazolium salt **4d** (923 mg, 76%) as a white solid.

mp 154.0–155.5 ºC [acetone/Et_2O (vapor diffusion), colorless prisms];

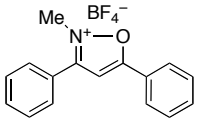
^{1}H NMR (400 MHz, acetone-d_6) δ 1.44 (s, 9H), 1.57 (s, 9H), 4.57 (s, 3H), 7.18 (s, 1H);

^{13}C NMR (100 MHz, acetone-d_6) δ 28.2, 28.3, 33.9, 34.4, 42.0, 105.3, 170.3, 183.5;

IR (ATR) 3418, 2976, 1595, 1525, 1467, 1372, 1258, 1033 cm^{-1};

Anal. Calc'd for $C_{12}H_{22}BF_4NO$: C, 50.91; H, 7.83; N, 4.95; Found: C, 50.70; H, 8.00; N, 4.82.

(Table 1, entry 4)



4e

Prepared according to the general procedure from isoxazole **3e** (2.21 g, 10.0 mmol) and trimethyloxonium tetrafluoroborate (90%, 1.78 g, 11 mmol) under the conditions indicated in Table 1. The crude product was purified by trituration with Et_2O to give isoxazolium salt **4e** (3.08 g, 95%) as a white solid.

mp 231.0–232.0 ºC [acetone/Et_2O (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, acetone-d_6) δ 4.69 (s, 3H), 7.70–7.74 (m, 2H), 7.77–7.82 (m, 3H), 7.83–7.87 (m, 1H), 8.04–8.07 (m, 2H), 8.10 (s, 1H), 8.15–8.18 (m, 2H);

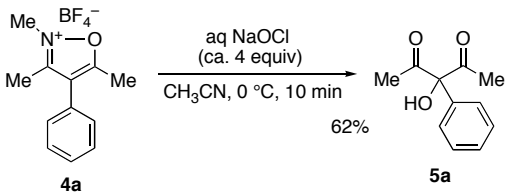
^{13}C NMR (100 MHz, acetone-d_6) δ 40.4, 104.9, 122.5, 123.0, 127.0, 129.6, 129.7, 129.9, 133.6, 133.9, 159.4, 169.3;

IR (ATR) 3134, 1608, 1576, 1542, 1489, 1465, 1427, 1049, 1037 cm^{-1};

Anal. Calc'd for $C_{16}H_{14}BF_4NO$: C, 59.48; H, 4.37; N, 4.34; Found: C, 59.58; H, 4.57; N, 4.36.

General procedure for oxidation of isoxazolium salts with NaOCl

(Scheme 2)



4a **5a**

To a solution of isoxazolium salt **4a** (279 mg, 1.01 mmol) in acetonitrile (3 mL) was added aqueous NaOCl [5% (w/v), pH ca. 12, 6.0 mL, ca. 4.0 mmol] at 0 °C and the mixture was stirred for 10 min at this temperature. The products were extracted with EtOAc (x3) and the combined organic extracts were washed with aqueous $Na_2S_2O_3$ [10% (w/v)] and brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by recycling preparative HPLC (column: JAIGEL-1H+2H, eluent: $CHCl_3$) to give

3-hydroxy-3-phenylpentane-2,4-dione[7] (**5a**, 120 mg, 62%) as colorless oil. This compound was gradually developed a yellow color on storage at 5 °C with slight decomposition.

R_f 0.7 (hexane/EtOAc = 3/1);

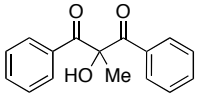
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 6H), 5.27 (s, 1H), 7.35–7.43 (m, 3H), 7.47–7.50 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 88.9, 125.7, 128.7, 128.8, 136.4, 205.8;

IR (neat) 3427, 3063, 3029, 2929, 1965, 1902, 1715, 1493, 1450, 1418, 1356, 1172, 1105, 1073, 757, 702 cm^{-1};

HRMS (EI-MS) calc'd for $C_{11}H_{12}O_3$: [M^+] 192.0786; Found: 192.0756.

(Table 1, entry 1)



5b

Prepared according to the general procedure from isoxazolium salt **4b** (337 mg, 1.00 mmol) with aqueous NaOCl [5% (w/v), 6.0 mL, ca. 4.0 mmol] under the conditions indicated in Table 1. The crude product was purified by silica-gel column chromatography (hexane/EtOAc = 4/1) to give 2-hydroxy-1,3-diketone **5b** (186 mg, 73%) as a yellow sticky solid. Recrystallization from hexane at 5 °C gave colorless needles. This compound was gradually developed a yellow color on storage at 5 °C with slight decomposition.

R_f 0.5 (hexane/EtOAc = 4/1);

mp 103.5–105.5 ºC [hexane (5 °C), colorless needles];

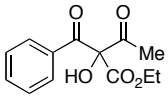
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.83 (s, 3H), 5.20 (s, 1H), 7.35–7.39 (m, 4H), 7.47–7.52 (m, 2H), 7.92–7.95 (m, 4H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6, 84.2, 128.6, 129.7, 133.8, 133.9, 197.8;

IR (ATR) 3428, 1667, 1597, 1449, 1234, 1147, 956 cm^{-1};

Anal. Calc'd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55; Found: C, 75.36; H, 5.34.

(Table 1, entry 2)



5c

To a solution of isoxazole **3c** (513 mg, 2.22 mmol) in CH_2Cl_2 (4.4 mL), trimethyloxonium tetrafluoroborate (90%, 406 mg, 2.5 mmol) was added at 0 °C, and the mixture was allowed to warm to room temperature. After stirring for 18 h, MeOH was added to the mixture and concentration in vacuo followed by washing with Et_2O (x2) gave the crude product as an oil. To a solution of the resulting product in CH_3CN (7.3 mL) was added aqueous NaOCl [5% (w/v), 13.2 mL, ca. 8.9 mmol] at 0 °C and the mixture was stirred for 10 min at this temperature. The products were extracted with Et_2O (x3) and the combined organic extracts were washed with aqueous $Na_2S_2O_3$ [10% (w/v)], brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (hexane/EtOAc = 6/1 to 4/1) to give 2-hydroxy-1,3-diketone **5c**

[7] J. E. Baldwin, O. W. Lever, Jr., N. R. Tzodikov, *J. Org. Chem.* **1976**, *41*, 2874–2877.

(444 mg, 80%) as yellow oil.

R_f 0.4 (hexane/EtOAc = 4/1);

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, 3H, *J* = 7.1 Hz), 2.47 (s, 3H), 4.32 (q, 2H, *J* = 7.1 Hz), 5.09 (s, 1H), 7.43–7.47 (m, 2H), 7.56–7.81 (m, 1H), 7.96–7.99 (m, 2H);

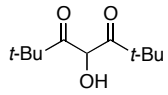
^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 26.1, 63.0, 88.0, 128.4, 129.7, 133.3, 133.8, 167.5, 192.5, 201.1;

IR (neat) 3430, 2985, 1748, 1725, 1684, 1598, 1449, 1360, 1258, 1235, 1132 cm^{-1};

LRMS (EI-MS) calc'd for $C_{13}H_{14}O_5$: [M^+] 250; Found: 250, 208, 134, 105 (base peak);

HRMS (EI-MS) calc'd for $C_{13}H_{14}O_5$: [M^+] 250.0841; Found: 250.0817.

(Table 1, entry 3)



5d

Prepared according to the general procedure from isoxazolium salt **4d** (420 mg, 1.57 mmol) with aqueous NaOCl [5% (w/v), 9.3 mL, ca. 6.2 mmol] under the conditions indicated in Table 1. The crude product was purified by silica-gel column chromatography (hexane/EtOAc = 9/1) to give 2-hydroxy-1,3-diketone **5d** (265 mg, 84%) as colorless oil. This compound was crystallized at 5 °C and gradually developed a yellow color on storage at 5 °C with no spectral change.

R_f 0.55 (hexane/EtOAc = 4/1);

mp 42.5–44.0 ºC [crystallization at 5 °C, colorless prisms];

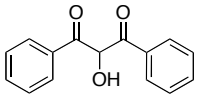
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 18H), 4.12 (d, 1H, *J* = 6.8 Hz), 5.27 (d, 1H, *J* = 6.8 Hz);

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 43.7, 74.7, 211.8;

IR (ATR) 3433, 2970, 2875, 1715, 1699, 1481, 994 cm^{-1};

Anal. Calc'd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07; Found: C, 66.16; H, 9.84.

(Table 1, entry 4)



5e

Prepared according to the general procedure from isoxazolium salt **4e** (323 mg, 1.00 mmol) with aqueous NaOCl [5% (w/v), 6.0 mL, ca. 4.0 mmol] in the presence of pyridine (0.32 mL, 4.0 mmol) under the conditions indicated in Table 1. The crude product was washed with hexane to afford 2-hydroxy-1,3-diketone **5e** (202 mg, 84%) as a white solid.

R_f 0.55 (hexane/EtOAc = 4/1);

mp 103.0–104.5 ºC [EtOAc/hexane (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (d, 1H, *J* = 5.9 Hz), 6.10 (d, 1H, *J* = 5.9 Hz), 7.44–7.48 (m, 4H), 7.57–7.62 (m, 2H), 7.98–8.01 (m, 4H);

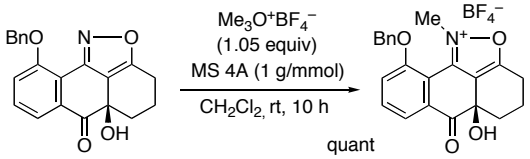
^{13}C NMR (100 MHz, $CDCl_3$) δ 78.4, 128.8, 129.2, 134.1, 134.2, 195.6;

IR (ATR) 3356, 3068, 2918, 1688, 1676, 1596, 1447, 1294, 1228, 1202, 1180, 1095 cm^{-1};

Anal. Calc'd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03; Found: C, 75.27; H, 5.21.

General procedure for hydroxylation of polycyclic isoxazolium salts

(Scheme 3)



To a mixture of isoxazole (*R*)-**6** (413 mg, 1.19 mmol, 98% ee) and MS 4A (2.38 g) in CH_2Cl_2 (12 mL), trimethyloxonium tetrafluoroborate (90%, 215 mg, 1.3 mmol) was added at 0 °C, and the mixture was allowed to warm to room temperature. After stirring for 10 h, MeOH was added to the mixture. The mixture was filtered through Celite® pad and the filtrates were concentrated under reduced pressure. The residue was triturated with Et_2O followed by filtration to give isoxazolium salt **7a** (531 mg, quant) as an off-white solid.

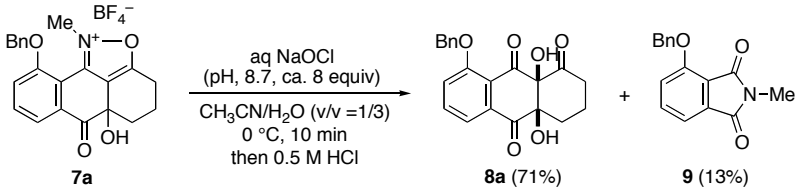
mp 131.0–134.0 ºC [acetone/Et_2O (vapor diffusion), light yellow prisms];

^{1}H NMR (400 MHz, DMSO-d_6) δ 1.59–1.65 (m, 1H), 2.06–2.23 (m, 3H), 2.76–2.85 (m, 1H), 3.07–3.13 (m, 1H), 4.24 (s, 3H), 5.45 (d, 1H, *J* = 11.2 Hz), 5.51 (d, 1H, *J* = 11.2 Hz), 6.79 (brs, 1H), 7.41–7.48 (m, 3H), 7.58 (brd, 2H, *J* = 6.8 Hz), 7.68 (d, 1H, *J* = 7.6 Hz), 7.83 (d, 1H, *J* = 8.5 Hz), 7.98 (dd, 1H, J = 8.5, 7.6 Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ 16.6, 21.7, 27.7, 43.7, 65.8, 71.3, 110.1, 118.3, 119.2, 122.0, 128.7, 134.6, 134.8, 137.1, 150.9, 155.4, 173.8, 192.7;

IR (KBr) 3489, 3152, 2958, 1720, 1653, 1579, 1498, 1275, 1061, 999, 903, 847, 806, 758 cm^{-1};

Anal. Calc'd for $C_{22}H_{20}BF_4NO_4$: C, 58.82; H, 4.49; N, 3.12; Found: C, 58.61; H, 4.78; N, 3.36.



The optimized conditions (Table 2, entry 6) are described as the following. The pH of commercial NaOCl (pH ca. 12) was adjusted to pH 8.7 by careful addition of conc. HCl at 0 °C. To a mixture of isoxazolium salt **7a** (108 mg, 0.241 mmol) in CH_3CN (1.2 mL) and water (3.6 mL), pH-adjusted NaOCl [5% (w/v), pH 8.7, 2.9 mL, ca. 1.9 mmol] was added dropwise at 0 °C. After stirring for 10 min, the products were extracted with EtOAc (x3). The combined organic extracts were washed with aqueous $Na_2S_2O_3$ [10% (w/v)], 0.5 M HCl, and brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (EtOAc/hexane/CF_3COOH = 100/200/0.1) to give diol **8a** (63.0 mg, 71%) as a yellow solid and phthalimide **9** (8.2 mg, 13%) as a white solid.

Diol **8a**

R_f 0.4 (hexane/EtOAc = 1/1);

mp 210.0 ºC [decomp, acetone/hexane (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.94–2.06 (m, 2H), 2.18 (ddd, 1H, *J* = 13.5, 13.2, 3.6 Hz), 2.27–2.35 (m, 1H), 2.70–2.76 (m, 1H), 2.90 (ddd, 1H, *J* = 15.0, 13.2, 7.0 Hz), 3.72 (brs, 1H), 4.65 (s, 1H), 5.23 (d, 1H, *J* = 12.1 Hz), 5.30 (d, 1H, *J* = 12.1 Hz), 7.31–7.43 (m, 4H), 7.51 (brd, 2H, *J* = 7.3 Hz), 7.72 (dd, 1H, *J* = 7.7, 7.7 Hz), 7.79 (dd, 1H, *J* = 7.7, 1.0 Hz);

^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 32.9, 37.9, 71.1, 82.4, 86.2, 120.0, 120.2, 122.2, 126.7, 128.2, 128.8, 134.2, 135.5, 135.9, 159.5, 191.3, 196.5, 205.2;

IR (KBr) 3437, 3095, 2956, 1728, 1689, 1585, 1450, 1309, 1284, 1211, 1126, 1061, 1028, 964 cm^{-1};

Anal. Calc'd for $C_{21}H_{18}O_6$: C, 68.85; H, 4.95; Found: C, 68.65; H, 4.71;

Crystallographic data: $C_{21}H_{18}O_6$, MW = 366.35, 0.40 x 0.20 x 0.10 mm, monoclinic, space group $P2_1/c$, $Z = 4$, T = 173 K, a = 9.8268(7), b = 10.1985(7), c = 17.0680(2) Å, V = 1690.6(3) Å^3, λ(Mo Kα) = 0.71075 Å, μ = 0.106 mm^{-1}. Intensity data were collected on Rigaku RAXIS-RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 36343 reflections were measured and 5927 were independent. Final $R1$ = 0.0449, $wR2$ = 0.1121 (5197 refs; $I > 2\sigma(I)$), and GOF = 1.082 (for all data, $R1$= 0.0588, $wR2$ = 0.1280).

CCDC 679882 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.

Phthalimide **9**

R_f 0.6 (hexane/EtOAc = 1/1);

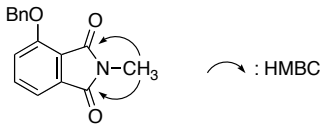
mp 122.0–123.0 ºC [acetone/Et_2O (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.16 (s, 3H), 5.35 (s, 2H), 7.18 (d, 1H, *J* = 8.5 Hz), 7.30–7.59 (m, 7H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 70.8, 115.7, 118.1, 119.4, 126.7, 128.1, 128.7, 134.5, 135.75, 135.84, 155.5, 166.9, 168.1;

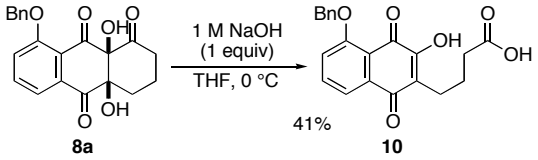
IR (KBr) 3076, 3032, 2939, 2883, 1763, 1711, 1608, 1487, 1444, 1429, 1387, 1277, 1045, 972 cm^{-1};

Anal. Calc'd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24; Found: C, 72.12; H, 5.13; N, 5.39.



HMBC correlations for phthalimide **9**

***retro*-Claisen decomposition of diol 8a**



To a solution of diol **8a** (21.1 mg, 0.058 mmol) in THF (0.5 mL) was added 1 M NaOH (50 μL, 0.05 mmol) at 0 °C. The resulting red solution was stirred for 1 h before quenching by addition of 1 M HCl. The products were extracted with EtOAc (x2) and the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by PTLC (eluent: EtOAc) to afford carboxylic acid **10** (8.7 mg, 41%) as a yellow solid.

mp 158.0–159.0 ºC [acetone/hexane (vapor diffusion), yellow prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (tt, 2H, *J* = 7.6, 7.6 Hz), 2.41 (t, 2H, *J* = 7.6 Hz), 2.65 (t, 2H, *J* = 7.6 Hz), 5.31 (s, 2H), 7.27 (d, 1H, *J* = 7.6 Hz Hz), 7.34 (t, 1H, *J* = 7.8 Hz), 7.42 (dd, 2H, *J* = 7.8, 7.1 Hz), 7.55 (d, 2H, *J* = 7.1 Hz), 7.65 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.80 (d, 1H, *J* = 7.6 Hz), 7.81 (brs, 1 H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 23.0, 33.5, 71.0, 117.4, 118.2, 120.0, 120.7, 126.8, 128.2, 128.8, 135.2, 135.8, 136.2, 154.0, 159.0, 178.1, 179.5, 184.4;

IR (KBr) 3454, 3261, 2937, 1714, 1699, 1655, 1637, 1581, 1446, 1371, 1288, 1228, 1203, 1101 cm^{-1};

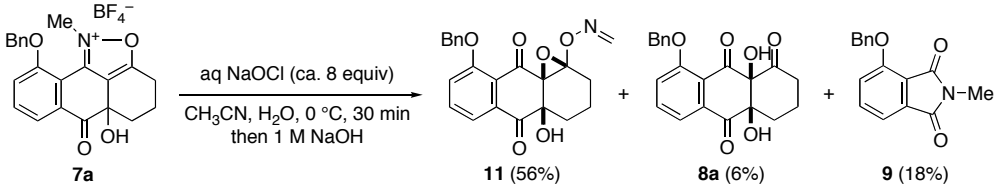
Anal. Calc'd for $C_{21}H_{18}O_6$: C, 68.85; H, 4.95; Found: C, 68.61; H, 5.10.

Crystallographic data: $C_{21}H_{18}O_6 \cdot C_3H_6O$, MW = 424.43(sum), 0.50 x 0.20 x 0.05 mm, monoclinic, space group $P2_1/c$, Z = 4, T = 293 K, a = 5.0994(2), b = 14.8630(15), c = 28.4173(14) Å, V = 2153.5(3) Å^3, λ(Mo Kα) = 0.71074 Å, μ = 0.096 mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 20556 reflections were measured and 4978 were independent. Final $R1$ = 0.0479, $wR2$ = 0.1253 (3815 refs; $I > 2\sigma(I)$), and GOF = 1.030 (for all data, $R1$ = 0.0641, $wR2$ = 0.1383).

CCDC 679884 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.

Trapping of the intermediary epoxide 11

(Scheme 4)



To a mixture of isoxazolium salt **7a** (162 mg, 0.360 mmol) in CH_3CN (3.6 mL) and water (10.8 mL) was added aqueous NaOCl [5% (w/v), pH ca. 12, 4.3 mL, ca. 2.9 mmol] at 0 °C. After stirring for 30 min at this

temperature, aqueous NaOH (1 M, 1.0 mL) was added to the mixture and the products were extracted with EtOAc (x3). The combined organic layer was washed with brine, dried over Na_2SO_4 concentrated under reduced pressure. The residue was triturated with Et_2O followed by filtration to afford epoxide **11** (80.0 mg, 56%) as an off-white solid. After concentration of the filtrate, the residue was purified by PTLC (hexane/EtOAc = 1/1) to give diol **8a** (8.0 mg, 6%) and phthalimide **9** (17.3 mg, 18%). Recrystallization of **11** from acetone/toluene gave a single crystal for X-ray analysis.

R_f 0.35 (hexane/EtOAc = 1/1);

mp 174.0 ºC [decomp, acetone/toluene (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, acetone-d_6) δ 1.42–1.58 (m, 2H), 1.66–1.74 (m, 1H), 2.19–2.23 (m, 2H), 2.36–2.40 (m, 1H), 5.28 (d, 1H, J = 12.6 Hz), 5.36 (d, 1H, J = 12.6 Hz), 5.58 (s, 1H), 6.61 (d, 1H, J = 6.8 Hz), 6.90 (d, 1H, J = 6.8 Hz), 7.28–7.40 (m, 3H), 7.57–7.62 (m, 3H), 7.76–7.81 (m, 2H);

^{13}C NMR (100 MHz, acetone-d_6) δ 18.8, 26.8, 27.7, 71.3, 71.8, 92.2, 120.8, 121.1, 125.8, 127.7, 128.4, 129.2, 135.7, 136.7, 137.8, 142.3, 158.6, 185.4, 193.2, 206.1;

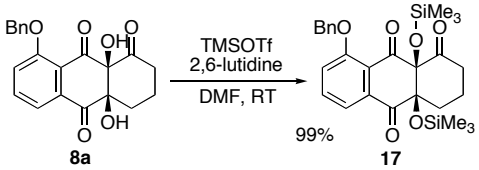
IR (KBr) 3390, 2941, 1697, 1585, 1500, 1440, 1379, 1298, 1230, 935 cm^{-1};

Anal. Calc'd for $C_{22}H_{19}NO_6$: C, 67.17; H, 4.87; N, 3.56; Found: C, 67.06; H, 5.09; N, 3.70;

Crystallographic data: $C_{22}H_{19}NO_6$, MW = 393.38, 0.55 x 0.45 x 0.35 mm, triclinic, space group P–1, Z = 2, T = 223 K, a = 9.660(2), b = 9.948(19), c = 10.480(19) Å, V = 941.0(3) Å^3, λ(Mo Kα) = 0.71075 Å, μ = 0.102 mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 9089 reflections were measured and 4230 were independent. Final $R1$ = 0.0512, $wR2$ = 0.1621 (3536 refs; $I > 2\sigma(I)$), and GOF = 1.213 (for all data, $R1$= 0.0581, $wR2$ = 0.1712).

CCDC 679883 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.

Silylation of *cis*-diol 8a



To a mixture of diol **8a** (96.0 mg, 0.262 mmol) and 2,6-lutidine (122 μL, 1.05 mmol) in DMF (33 mL) was added a DMF solution (2.6 mL) of TMSOTf (189 μL, 1.05 mmol) dropwise at 0 °C. The reaction was warmed to room temperature. After stirring for 7 h, the reaction was quenched with saturated NH_4Cl, and the products were extracted with Et_2O (x3). The combined organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by PTLC (EtOAc/hexane = 1/3) to give bistrimethylsilylether **17** (130 mg, 97%, 98% ee) as a white solid. The enantiomeric excess was assessed

by HPLC analysis on a chiral stationary phase [CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 1:99, flow rate: 1.0 mL/min, 25 °C: t_1 = 9.5 min (minor); t_2 = 10.5 min (major)].

R_f 0.6 (hexane/EtOAc = 2/1);

mp 108.0–110.5 ºC (precipitation from EtOAc/hexane);

^{1}H NMR (400 MHz, $CDCl_3$) δ –0.01 (brs, 9H), 0.17 (s, 9H), 1.83–1.90 (m, 2H), 2.00–2.08 (m, 1H), 2.13–2.25 (m, 1H), 2.57–2.62 (m, 1H), 2.76–2.85 (m, 1H), 5.23 (d, 1H, *J* = 12.5 Hz), 5.31 (d, 1H, *J* = 12.5 Hz), 7.29–7.40 (m, 4H), 7.47–7.50 (m, 2H), 7.65 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.77 (d, 1H, *J* = 7.6 Hz);

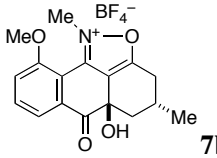
^{13}C NMR (100 MHz, $CDCl_3$) δ 1.8, 2.4, 20.6, 34.0, 39.4, 70.8, 86.7, 91.0, 119.1, 119.7, 122.7, 126.5, 127.9, 128.5, 134.0, 134.9, 135.6, 158.4, 193.4, 195.7, 204.6;

IR (ATR) 2955, 1733, 1710, 1683, 1583, 1462, 1242, 1210, 1115, 974, 832 cm^{-1};

Anal. Calc'd for $C_{27}H_{34}O_6Si_2$: C, 63.50; H, 6.71; Found: C, 63.70; H, 6.93;

Optical rotation $[\alpha]_D^{26}$ +18.4 ($CHCl_3$, *c* 1.01) for 98% ee.

(Table 3, entry 1)



7b

Prepared according to the general procedure from the corresponding isoxazole (913 mg, 3.20 mmol), trimethyloxonium tetrafluoroborate (90%, 552 mg, 3.4 mmol) and MS 4A (3.2 g) in CH_2Cl_2 (64 mL) at room temperature for 9 h. The crude product was triturated with Et_2O followed by filtration to afford isoxazolium salt **7b** (1.21 g, 98%) as a white solid.

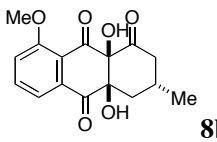
mp 205.0 ºC [decomp, acetone/Et_2O (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, DMSO-d_6) δ 1.22 (d, 3H, *J* = 6.0 Hz), 1.50 (dd, 1H, *J* = 13.0, 13.0 Hz), 2.10 (brd, 1H, *J* = 13.0 Hz), 2.41–2.50 (m, 2H), 3.24–3.30 (m, 1H), 4.11 (s, 3H), 4.46 (s, 3H), 6.81 (s, 1H), 7.66 (d, 1H, *J* = 7.5 Hz), 7.72 (d, 1H, *J* = 8.5 Hz), 7.98 (dd, 1H, *J* = 8.5, 7.5 Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ 20.4, 24.8, 29.1, 36.1, 43.6, 56.6, 66.0, 110.0, 118.34, 118.37, 121.9, 134.5, 137.3, 150.7, 156.3, 173.8, 192.6;

IR (KBr) 3471, 3101, 2962, 1728, 1658, 1579, 1498, 1281, 1254, 1072, 904, 781 cm^{-1};

Anal. Calc'd for $C_{17}H_{18}BF_4NO_4$: C, 52.74; H, 4.69; N, 3.62; Found: C, 52.97; H, 4.83; N, 3.43.



8b

Prepared according to the general procedure from isoxazolium salt **7b** (129 mg, 0.333 mmol) and pH-adjusted NaOCl [5% (w/v), pH 8.6, 3.6 mL, ca. 2.4 mmol] in CH_3CN (3.3 mL) and water (9.9 mL) at 0 °C. The organic

extracts were washed with 0.5 M HCl and brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The crude product was purified by trituration with Et_2O/hexane (v/v = 1/4) followed by filtration to afford diol **8b** (73.0 mg, 72%) as a white solid. The filtrate was concentrated under reduced pressure and the residue was purified by silica-gel column chromatography (EtOAc/hexane = 2/3) to afford diol **8b** (4.6 mg, 5%) as a white solid.

R_f 0.3 (hexane/EtOAc = 1/1);

mp 190.0–191.0 ºC [acetone/hexane (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (d, 3H, *J* = 6.3 Hz), 1.82–1.88 (m, 1H), 1.94–1.99 (m, 1H), 2.52–2.63 (m, 2H), 2.69–2.77 (m, 1H), 3.73 (brs, 1H), 4.00 (s, 3H), 4.59 (s, 1H), 7.33–7.38 (m, 1H), 7.74–7.78 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 29.1, 40.9, 45.9, 56.6, 81.8, 85.6, 118.3, 119.9, 121.4, 134.1, 136.0, 160.5, 191.6, 196.3, 204.2;

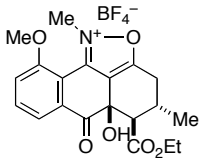
IR (ATR) 3455, 2949, 2841, 1726, 1699, 1686, 1584, 1275, 1205, 1051, 967 cm^{-1};

Anal. Calc'd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30; Found: C, 63.37; H, 5.52;

Crystallographic data: $C_{16}H_{16}O_6$, MW = 304.29, 0.45 x 0.20 x 0.10 mm, triclinic, space group *P*–1, *Z* = 2, *T* = 173 K, *a* = 6.7103(16), *b* = 10.1430(3), *c* = 11.5770(3) Å, *V* = 704.9(3) Å^3, λ(Cu Kα) = 1.5487 Å, μ = 0.929 mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 7109 reflections were measured and 2490 were independent. Final *R*1 = 0.0687, *wR*2 = 0.1868 (1766 refs; $I > 2\sigma(I)$), and GOF = 1.192 (for all data, *R*1= 0.0901, *wR*2 = 0.1971).

CCDC 679885 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.

(Table 3, entry 2)



7c

Prepared according to the general procedure from the corresponding isoxazole (543 mg, 1.52 mmol), trimethyloxonium tetrafluoroborate (90%, 275 mg, 1.7 mmol) and MS 4A (1.5 g) in CH_2Cl_2 (15 mL) at room temperature for 12 h. The crude product was triturated with Et_2O followed by filtration to afford isoxazolium salt **7c** (710 mg, quant) as a white solid.

mp 180.0 ºC [decomp, acetone/Et_2O (vapor diffusion), colorless prisms];

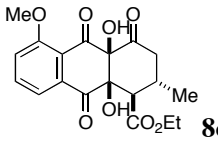
^{1}H NMR (400 MHz, DMSO-d_6) δ 1.13 (d, 3H, *J* = 6.3 Hz), 1.29 (t, 3H, *J* = 7.1 Hz), 2.59–2.77 (m, 3H), 3.35–3.41 (m, 1H), 4.11 (s, 3H), 4.23 (q, 2H, *J* = 7.1 Hz), 4.49 (s, 3H), 6.60 (brs, 1H), 7.65 (d, 1H, *J* = 7.3 Hz), 7.73 (d, 1H, *J* = 8.3 Hz), 7.98 (dd, 1H, *J* = 8.3, 7.3 Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ 14.1, 17.8, 28.0, 29.3, 44.0, 48.4, 56.7, 60.2, 68.1, 109.4, 118.0, 118.6, 122.1,

134.0, 137.4, 150.3, 156.4, 171.4, 172.0, 191.1;

IR (KBr) 3357, 3107, 2983, 1710, 1701, 1662, 1581, 1506, 1406, 1377, 1284, 1213, 1061, 910 cm^{-1};

Anal. Calc'd for $C_{20}H_{22}BF_4NO_6$: C, 52.31; H, 4.83; N, 3.05; Found: C, 52.23; H, 5.03; N, 2.89.



8c

Prepared according to the general procedure with isoxazolium salt **7c** (183 mg, 0.399 mmol) and pH-adjusted NaOCl [5% (w/v), pH 8.6, 4.8 mL, ca. 3.2 mmol] in CH_3CN (4 mL) and water (12 mL) at 0 °C. The organic extracts were washed with 0.5 M HCl and brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The crude product was purified by trituration with Et_2O followed by filtration to afford diol **8c** (34.6 mg, 23%) as a white solid. The filtrate was concentrated under reduced pressure and the residue was purified by PTLC (acetone/toluene = 1/3) to give diol **8c** (66.5 mg, 44%) and phthalimide **18**[8] (17.3 mg, 23%).

R_f 0.5 (hexane/EtOAc = 1/3);

mp 181.5–182.5 ºC [acetone/hexane (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (d, 3H, J = 6.1 Hz), 1.16 (t, 3H, J = 7.1 Hz), 2.60–2.67 (m, 1H), 2.77–2.89 (m, 2H), 2.93 (d, 1 H, J = 11.2 Hz), 3.99–4.14 (m, 2H), 4.01 (s, 3H), 4.04 (s, 1H), 4.55 (s, 1H), 7.38 (dd, 1H, J = 8.3, 0.6 Hz), 7.73 (dd, 1H, J = 7.3, 0.6 Hz), 7.80 (dd, 1H, J = 8.3, 7.3 Hz);

^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 20.1, 30.8, 44.4, 54.6, 56.6, 61.3, 83.0, 85.5, 118.3, 119.8, 121.0, 134.6, 136.3, 160.6, 168.6, 190.8, 194.8, 202.6;

IR (ATR) 3429, 2981, 2952, 1739, 1722, 1702, 1676, 1584, 1471, 1278, 1220, 1101, 1033, 1018, 967 cm^{-1};

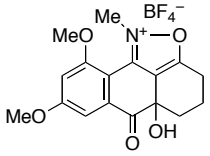
Anal. Calc'd for $C_{19}H_{20}O_8$: C, 60.63; H, 5.36; Found: C, 60.72; H, 5.59.

Crystallographic data: $C_{19}H_{20}O_8$, MW = 376.35, 0.30 x 0.20 x 0.10 mm, triclinic, space group P–1, Z = 4, T = 103 K, a = 9.480(5), b = 11.457(4), c = 16.716(8) Å, V = 1713.3(13) $Å^3$, λ(Mo Kα) = 0.71075 Å, μ = 0.115 mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 16146 reflections were measured and 7577 were independent. Final $R1$ = 0.0647, $wR2$ = 0.1702 (5402 refs; $I > 2\sigma(I)$), and GOF = 1.019 (for all data, $R1$= 0.0830, $wR2$ = 0.1836).

CCDC 679886 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.

[8] A. de la Hoz, A. Díaz-Ortiz, A. M. Fraile, M. V. Gómez, J. A. Mayoral, A. Moreno, A. Saiz, E. Vázquez, *Synlett* **2001**, 753–756.

(Table 3, entry 3)



7d

Prepared according to the general procedure from the corresponding isoxazole (743 mg, 2.47 mmol), trimethyloxonium tetrafluoroborate (90%, 426 mg, 2.6 mmol) and MS 4A (2.4 g) in CH_2Cl_2 (49 mL) at 10 °C for 23 h. The crude product was triturated with CH_2Cl_2 to afford isoxazolium salt **7d** (942 mg, 95%) as a white solid.

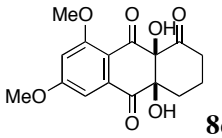
mp 185.0 ºC [decomp, acetone/Et_2O (vapor diffusion), colorless needles];

^{1}H NMR (400 MHz, DMSO-d_6) δ 1.59–1.66 (m, 1H), 2.07–2.22 (m, 3H), 2.75–2.84 (m, 1H), 3.07–3.13 (m, 1H), 4.01 (s, 3H), 4.11 (s, 3H), 4.40 (s, 3H), 6.75 (brs, 1H), 7.16–7.18 (m, 2H);

^{13}C NMR (100 MHz, DMSO-d_6) δ 16.7, 21.5, 27.6, 43.4, 56.6, 56.9, 65.8, 102.9, 103.3, 108.3, 117.7, 136.1, 150.4, 158.5, 166.4, 172.7, 192.4;

IR (KBr) 3411, 3170, 2943, 1718, 1653, 1597, 1489, 1356, 1300, 1157, 1084 cm^{-1};

Anal. Calc'd for $C_{17}H_{18}BF_4NO_5$: C, 50.65; H, 4.50; N, 3.47; Found: C, 50.86; H, 4.75; N, 3.63.



8d

Prepared according to the general procedure with isoxazolium salt **7d** (112 mg, 0.278 mmol) and aqueous NaOCl [5% (w/v), pH ca. 12, 3.2 mL, ca. 2.2 mmol] in CH_3CN (1.4 mL) and water (4.1 mL) at 0 °C. After stirring for 1 min, the reaction was quenched by the addition of aqueous $Na_2S_2O_3$ [10% (w/v)]. The organic extracts were washed with 0.5 M HCl and brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The crude product was purified by trituration with Et_2O followed by filtration to afford diol **8d** (45.0 mg, 51%) as a white solid. The filtrate was concentrated under reduced pressure and the residue was purified by PTLC (EtOAc/CH_2Cl_2/hexane = 3/2/1) to give diol **8d** (9.5 mg, 11%) and phthalimide **19** (11.5 mg, 19%).

R_f 0.4 (hexane/EtOAc/CH_2Cl_2 = 1/2/2);

mp 199.0–202.0 ºC [acetone/Et_2O (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92–2.04 (m, 2H), 2.17 (ddd, 1H, J = 13.0, 13.0, 3.1 Hz), 2.23–2.35 (m, 1H), 2.67–2.73 (m, 1H), 2.83 (ddd, 1H, J = 14.7, 13.0, 6.8 Hz), 3.68 (brs, 1H), 3.95 (s, 3H), 3.97 (s, 3H), 4.65 (s, 1H), 6.79 (d, 1H, J = 2.4 Hz), 7.24 (d, 1H, J = 2.4 Hz);

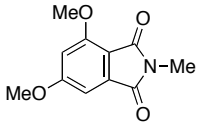
^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 33.0, 37.8, 56.2, 56.5, 82.4, 86.0, 103.6, 105.2, 115.8, 136.2, 162.8, 165.6, 190.5, 196.6, 205.2;

IR (ATR) 3452, 3396, 3017, 2943, 1727, 1698, 1676, 1595, 1558, 1447, 1328, 1236, 1192, 1161, 1150, 1130, 1081, 1057, 1021, 936, 854, 827 cm^{-1};

Anal. Calc'd for $C_{16}H_{16}O_7$: C, 60.00; H, 5.04; Found: C, 60.21; H, 5.19;

Crystallographic data: $C_{16}H_{16}O_7$, MW = 320.29, 0.45 x 0.40 x 0.20 mm, monoclinic, space group $P2_1/c$, $Z = 8$, $T = 173$ K, $a = 10.4221(12)$, $b = 7.2307(9)$, $c = 19.1640(2)$ Å, $V = 1425.8(3)$ Å^3, λ(Cu Kα) = 1.54187 Å, $\mu = 1.003$ mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 13649 reflections were measured and 2604 were independent. Final $R1 = 0.0694$, $wR2 = 0.2027$ (2364 refs; $I > 2\sigma(I)$), and GOF = 1.773 (for all data, $R1 = 0.0749$, $wR2 = 0.2050$).

CCDC 679887 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.



19

R_f 0.7 (hexane/EtOAc/CH_2Cl_2 = 1/2/2);

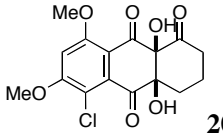
mp 191.5–192.5 ºC (acetone, colorless needles);

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12 (s, 3H), 3.92 (s, 3H), 3.97 (s, 3H), 6.62 (d, 1H, J = 1.8 Hz), 6.70 (d, 1H, J = 1.8 Hz);

^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 56.2, 56.3, 100.3, 103.5, 110.5, 136.4, 157.8, 166.3, 166.8, 168.0;

IR (ATR) 2974, 2949, 2843, 1760, 1698, 1616, 1593, 1496, 1445, 1428, 1375, 1327, 1223, 1208, 1157, 1076, 1035, 1016, 984, 843 cm^{-1};

Anal. Calc'd for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33; Found: C, 43.53; H, 4.01; N, 4.52.



20

Prepared according to the general procedure with isoxazolium salt **7d** (148 mg, 0.368 mmol) and pH-adjusted NaOCl [5% (w/v), pH 8.6, 4.4 mL, ca. 2.9 mmol] in acetone (4.9 mL) and water (9.8 mL) at 0 °C. The crude product was purified by silica-gel column chromatography (EtOAc/CH_2Cl_2/hexane/CF_3COOH = 200/200/150/ca. 0.2) to give diol **20** (59.9 mg, 46%) as an off-white solid and phthalimide **21** (10.9 mg, 12%) as a white solid.

R_f 0.4 (hexane/EtOAc = 1/3);

mp 170.0–171.0 ºC [acetone/Et_2O (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, acetone-d_6) δ 1.88–1.93 (m, 1H), 1.95–2.28 (m, 3H), 2.46–2.52 (m, 1 H), 2.65 (ddd, 1 H, J = 14.4, 12.7, 6.8 Hz), 4.01 (s, 3H), 4.11 (s, 3H), 4.94 (brs, 1H), 5.41 (brs, 1H), 7.18 (s, 1H);

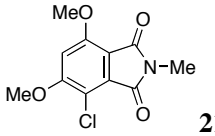
^{13}C NMR (100 MHz, acetone-d_6) δ 22.1, 32.3, 39.0, 57.0, 57.6, 84.2, 87.3, 102.1, 113.9, 116.2, 134.4, 162.3, 162.7, 189.8, 196.6, 204.8;

IR (ATR) 3623, 3452, 2941, 1722, 1663, 1573, 1542, 1476, 1432, 1347, 1309, 1243, 1215, 1190, 1066, 1023, 977, 942, 840 cm^{-1};

Anal. Calc'd for $C_{16}H_{15}ClO_7$: C, 54.17; H, 4.26; Found: C, 54.37; H, 4.50;

Crystallographic data: $C_{16}H_{15}ClO_7 \cdot 1/2H_2O$, MW = 363.74, 0.35 x 0.35 x 0.10 mm, monoclinic, space group *C2/c*, $Z = 8$, $T = 173$ K, $a = 17.758(4)$, $b = 8.910(6)$, $c = 21.527(17)$ Å, $V = 3145(3)$ $Å^3$, λ(Cu Kα) = 1.54186 Å, μ = 2.497 mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 16139 reflections were measured and 2862 were independent. Final $R1 = 0.0332$, $wR2 = 0.0829$ (2383 refs; $I > 2\sigma(I)$), and GOF = 1.046 (for all data, $R1 = 0.0412$, $wR2 = 0.0847$).

CCDC 679888 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.



21

R_f 0.6 (hexane/EtOAc = 1/3);

mp 207.0–208.0 ºC [acetone/Et_2O (vapor diffusion), colorless prisms];

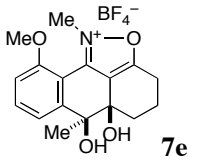
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13 (s, 3H), 4.02 (s, 3H), 4.04 (s, 3H), 6.63 (s, 1H);

^{13}C NMR (100 MHz, acetone-d_6) δ 23.8, 57.0, 57.7, 102.3, 111.4, 111.5, 131.4, 157.7, 162.5, 165.5, 166.1;

IR (ATR) 2945, 2840, 1762, 1700, 1600, 1433, 1371, 1315, 1224, 1173, 1085, 993 cm^{-1};

Anal. Calc'd for $C_{11}H_{10}NO_4$: C, 51.68; H, 3.94; N, 5.48; Found: C, 51.54; H, 3.94; N, 5.22.

(Table 3, entry 4)



7e

Prepared according to the general procedure from the corresponding isoxazole (984 mg, 3.42 mmol) and trimethyloxonium tetrafluoroborate (90%, 591 mg, 3.6 mmol) in CH_2Cl_2 (68 mL) at room temperature. The crude product was triturated with Et_2O to afford isoxazolium salt **7e** (1.26 g, 95%) as a white solid.

mp 172.0–173.0 ºC [acetone/Et_2O (vapor diffusion), colorless needles];

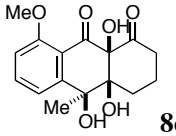
^{1}H NMR (400 MHz, DMSO-d_6) δ 1.15 (s, 3H), 1.76 (ddd, 1H, J = 13.2, 13.2, 3.4 Hz), 1.93–1.97 (m, 1H), 2.02–2.18 (m, 2H), 2.86 (m, 1H), 3.02–3.08 (m, 1H), 4.02 (s, 3H), 4.46 (s, 3H), 5.36 (brs, 1H), 5.45 (brs, 1H), 7.26 (d, 1H, J = 8.3 Hz), 7.55 (d, 1H, J = 7.6 Hz), 7.82 (dd, 1H, J = 8.3, 7.6 Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 21.7, 26.7, 27.4, 43.8, 56.1, 67.4, 76.6, 106.6, 111.2, 119.2, 119.5, 136.9,

150.0, 152.7, 156.5, 171.7;

IR (KBr) 3473, 2968, 1662, 1599, 1580, 1500, 1342, 1277, 1234, 1055, 804 cm^{-1};

Anal. Calc'd for $C_{17}H_{20}BF_4NO_4$: C, 52.47; H, 5.18; N, 3.60; Found: C, 52.24; H, 5.45; N, 3.41.



8e

Prepared according to the general procedure from isoxazolium salt **7e** (156 mg, 0.401 mmol) and aqueous NaOCl [5% (w/v), pH ca. 12, 4.7 mL, ca. 3.2 mmol] in CH_3CN (2 mL), and water (6 mL) at 0 °C. To a solution of the crude product in DMSO was added 1 M HCl at 0 °C. The products were extracted with $CHCl_3$ (x 3) and the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was triturated with Et_2O to afford triol **8e** (108 mg, 88%) as a white solid.

R_f 0.5 (hexane/EtOAc = 1/4);

mp 147.0–150.5 ºC (acetone/MeOH, colorless prisms);

^{1}H NMR (400 MHz, DMSO-d_6) δ 1.44–1.48 (m, 1H), 1.52 (s, 3H), 1.74–1.80 (m, 1H), 1.83–2.01 (m, 2H), 2.33–2.38 (m, 1H), 2.45–2.54 (m, 1H), 3.81 (s, 3H), 5.03 (s, 1H), 5.12 (brs, 1H), 6.97 (s, 1H), 7.14 (d, 1H, J = 8.0, 0.7 Hz), 7.34 (dd, 1H, J = 8.0, 0.7 Hz), 7.67 (dd, 1H, J = 8.0, 8.0 Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ 19.8, 22.3, 30.1, 38.4, 55.9, 74.6, 77.3, 86.8, 111.8, 116.9, 119.2, 135.6, 148.4, 160.2, 193.3, 206.6;

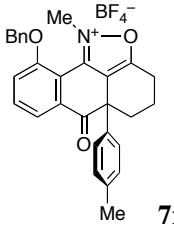
IR (ATR) 3433, 3376, 2964, 1735, 1655, 1591, 1572, 1466, 1445, 1429, 1376, 1245, 1074, 931 cm^{-1};

Anal. Calc'd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92; Found: C, 62.54; H, 5.89;

Crystallographic data: $C_{16}H_{18}O_6$, MW = 306.30, 0.40 x 0.38 x 0.16 mm, triclinic, space group P–1, Z = 2, T = 173 K, a = 8.191(4), b = 9.114(4), c = 10.136(7) Å, V = 691.2(7) $Å^3$, λ(Mo Kα) = 0.71075 Å, μ = 0.113 mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 6832 reflections were measured and 3124 were independent. Final $R1$ = 0.0741, $wR2$ = 0.2074 (2816 refs; $I > 2\sigma(I)$), and GOF = 1.913 (for all data, $R1$= 0.0780, $wR2$ = 0.2187).

CCDC 679889 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.

(Table 3, entry 5)



7f

Prepared according to the general procedure from the corresponding isoxazole (594 mg, 1.41 mmol), trimethyloxonium tetrafluoroborate (90%, 254 mg, 1.6 mmol) and MS 4A (1.4 g) in CH_2Cl_2 (28 mL) at room temperature. The crude product was triturated with Et_2O to afford isoxazolium salt **7f** (720 mg, 98%) as a white solid.

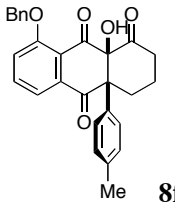
mp 164.0–165.0 ºC [acetone/Et_2O (vapor diffusion), colorless needles];

^{1}H NMR (400 MHz, DMSO-d_6) δ 1.40–1.52 (m, 1H), 1.96–2.10 (m, 2H), 2.20 (s, 3H), 2.40–2.43 (m, 1H), 2.82–2.92 (m, 1H), 3.03–3.10 (m, 1H), 4.32 (s, 3H), 5.43 (d, 1H, J = 11.3 Hz), 5.47 (d, 1H, J = 11.3 Hz), 7.11 (d, 2H, J = 8.7 Hz), 7.14 (d, 2H, J = 8.7 Hz), 7.43–7.48 (m, 4H), 7.57–7.59 (m, 2H), 7.74 (d, 1H, J = 8.5 Hz), 7.82 (dd, 1H, J = 8.5, 8.5 Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ 16.6, 20.3, 21.3, 30.5, 43.7, 51.2, 71.3, 110.1, 117.8, 119.4, 121.5, 126.9, 128.6, 128.7, 128.8, 129.6, 133.3, 134.8, 137.0, 137.9, 150.3, 155.2, 172.9, 194.6;

IR (KBr) 3068, 2930, 1711, 1649, 1577, 1496, 1458, 1281, 1254, 1057 cm^{-1};

Anal. Calc'd for $C_{29}H_{26}BF_4NO_3$: C, 66.56; H, 5.01; N, 2.68; Found: C, 66.35; H, 5.24; N, 2.44.



8f

Prepared according to the general procedure from isoxazolium salt **7f** (157 mg, 0.300 mmol) and pH-adjusted NaOCl [5% (w/v), pH 8.6, 3.6 mL, ca. 2.4 mmol] in CH_3CN (5.1 mL) and water (6.8 mL) at 0 °C. To a solution of crude product in THF was added 0.5 M HCl at 0 °C. After stirring for 10 min, the products were extracted with CH_2Cl_2 (x 3) and the combined organic layer was washed with brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by trituration with Et_2O/hexane (v/v = 1/4) followed by filtration to afford alcohol **8f** (105 mg, 79%) as a white solid. The filtrate was concentrated under reduced pressure and the residue was purified by PTLC (EtOAc/hexane = 1/1) to afford **8f** (10.6 mg, 8%) as an off-white solid.

R_f 0.4 (hexane/EtOAc/CH_2Cl_2 = 4/1/1);

mp 152.0–154.0 ºC [acetone/hexane (vapor diffusion), colorless prisms];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93–2.13 (m, 2H), 2.22 (s, 3H), 2.22–2.27 (m, 1H), 2.47 (ddd, 1H, J = 13.2, 13.2, 4.6 Hz), 2.65–2.70 (m, 1H), 3.12 (ddd, 1H, J = 13.4, 13.2, 7.3 Hz), 4.83 (s, 1H), 5.24 (d, 1H, J = 12.2 Hz), 5.28 (d,

1H, J = 12.2 Hz), 6.98 (d, 2H, J = 8.5 Hz), 7.18 (d, 2H, J = 8.5 Hz), 7.27–7.33 (m, 2H), 7.39 (dd, 2H, J = 7.5, 7.5 Hz), 7.50 (d, 2H, J = 7.5 Hz), 7.62 (dd, 1H, J = 8.0, 8.0 Hz), 7.78 (dd, 1H, J = 8.0, 0.7 Hz);

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 22.1, 30.4, 37.0, 64.6, 71.0, 84.8, 119.7, 120.1, 122.7, 126.6, 127.5, 127.9, 128.5, 129.1, 135.0, 135.5, 135.7, 137.3, 137.4, 157.8, 194.2, 195.6, 207.3;

IR (ATR) 3412, 3107, 3026, 2942, 2879, 1717, 1683, 1583, 1455, 1362, 1287, 1235, 1161, 1062, 942 cm^{-1};

Anal. Calc'd for $C_{28}H_{24}O_5$: C, 76.35; H, 5.49; Found: C, 76.23; H, 5.55;

Crystallographic data: $C_{28}H_{24}O_5$, MW = 440.47, 0.35 x 0.30 x 0.10 mm, monoclinic, space group $P2_1/a$, Z = 4, T = 173 K, a = 7.584(2), b = 19.878(5), c = 14.836(6) Å, V = 2158.5(11) $Å^3$, λ(Mo Kα) = 0.71075 Å, μ = 0.093 mm^{-1}. Intensity data were collected on Rigaku R-AXIS RAPID IP area detector system. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXL-97). A total of 20607 reflections were measured and 4888 were independent. Final $R1$ = 0.0556, $wR2$ = 0.1575 (4017 refs; $I > 2\sigma(I)$), and GOF = 1.270 (for all data, $R1$= 0.0651, $wR2$ = 0.1635).

CCDC 679890 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.