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COPPER(I) IODIDE-PROMOTED HYDROXYLATION ONTO THE LITHIUM OR POTASSIUM ENOLATE OF LACTONES AND LACTAMS

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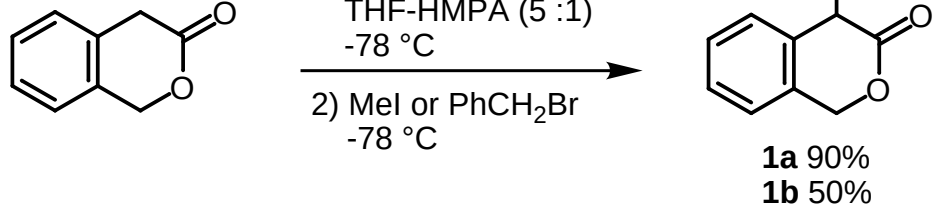
Abstract-After enolization of lactones (**1a**,**b**) and lactams (**2a**,**b**) with lithium or potassium hexamethyldisilazide in THF, each resultant enolate was treated with a solution prepared by mixing copper(I) iodide, pyridine, and *tert*-butyl hydroperoxide or *N*-methylmorpholine *N*-oxide in THF to give α-hydroxy lactones (**3a**,**b**) and α-hydroxy lactams (**4a**,**b**) in satisfied yields. This hydroxylation method was successfully applied to conversion of *dl*-desoxycamptothecin (*dl*-**7**) to *dl*-camptothecin (*dl*-**5**).

In the hydroxylation reactions at the α-methylene and α-methyne positions of various carbonyl

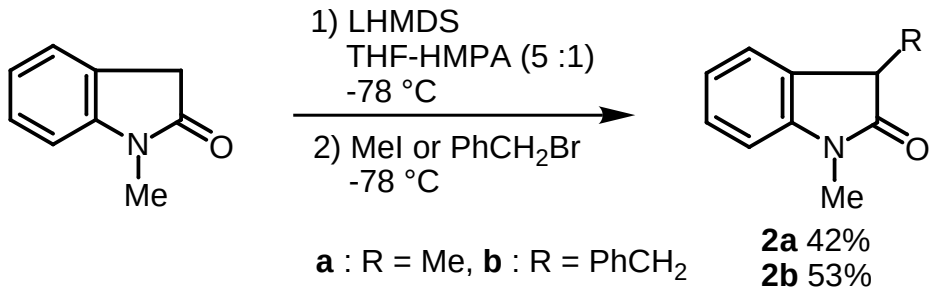
compounds, a large number of oxidations of the silyl enolates were performed by employing many oxidizing reagents such as osmium tetroxide together with 4-methylmorpholine *N*-oxide,[1a] chiral AD-mix-α and -β,[1b] chromyl chloride,[2] *m*-chloroperbenzoic acid,[3] dimethyldioxirane,[4] fructose-derived dioxirane,[5] chiral (salen)manganese(III) complexes,[6] singlet oxygen,[7] iodosobenzene-BF_3·OEt_2,[8] and *N*-sulfonyloxaziridines.[9] Similar oxidation reactions of the alkaline metal enolates of carbonyl compounds in order to obtain the α-hydroxy derivatives were also achieved by employing MoO_5·Py·HMPA (MoOPH),[10] achiral and chiral *N*-sulfonyloxaziridines,[11] dimethyldioxirane,[4,12] and benzeneseleninic anhydride,[13] respectively. There have been some reports of oxidative hydroxylation at the α-position of lactams and lactones using $CuCl_2$-O_2,[14] cobalt(II) Schiff's base complexes-O_2,[15] LDA or lithium hexamethyldisilazide (LHMDS)-MoOPH,[16] and LHMDS or potassium hexamethyldisilazide (KHMDS)-*N*-sulfonyloxaziridines.[11a] However, most of above hydroxylations of the lactams and lactones were exploited only for the one-step reaction in the total synthesis of natural products except for a few cases.[11a,15]

We now report direct hydroxylation reactions onto the lithium and/or potassium enolates of lactones (**1a**,**b**), lactams (**2a**,**b**), and *dl*-desoxycamptothecin (*dl*-**7**) by employing copper(I) iodide (CuI) and an oxidizing reagent, *tert*-butyl hydroperoxide (*t*-BuOOH) or *N*-methylmorpholine *N*-oxide (NMO). The compounds (**1a**,**b** and **2a**,**b**), precursors of hydroxylation, were prepared by treatment of commercially available isochroman-3-one and 1-methylindolin-2-one with *n*-BuLi or LHMDS and then methyl iodide or benzyl bromide in THF-HMPA (5 : 1), as shown in Scheme 1.

Scheme 1



1a 90%
1b 50%



First of all, hydroxylation of 4-methyl-2-benzopyran-3-one (**1a**) was attempted as follows. To a mixture of CuI, pyridine, and *t*-BuOOH in THF was added a THF solution of the lithium enolate generated by treatment of **1a** with LHMDS in THF utilizing a cannula system. The whole mixture was stirred at -78 °C for 36 h to give desired 4-hydroxy-4-methyl-2-bezopyran-3-one (**3a**) in 77% yield, as shown in Scheme 2 and Table 1 (Entry 1). Because the similar treatment of other compounds (**1b** and **2a**,**b**) resulted in 20-30% yields of the corresponding α-hydroxy lactone (**3b**) and α-hydroxy lactams (**4a**,**b**), their reactions were tentatively carried out by employing two times amounts of *t*-BuOOH and pyridine (except for Entry 2) in comparison with the case of **1**. The yields of **3b** and **4a**,**b** were improved to be 38-80%, as shown in Table 1 (Entries 2-4).

Scheme 2

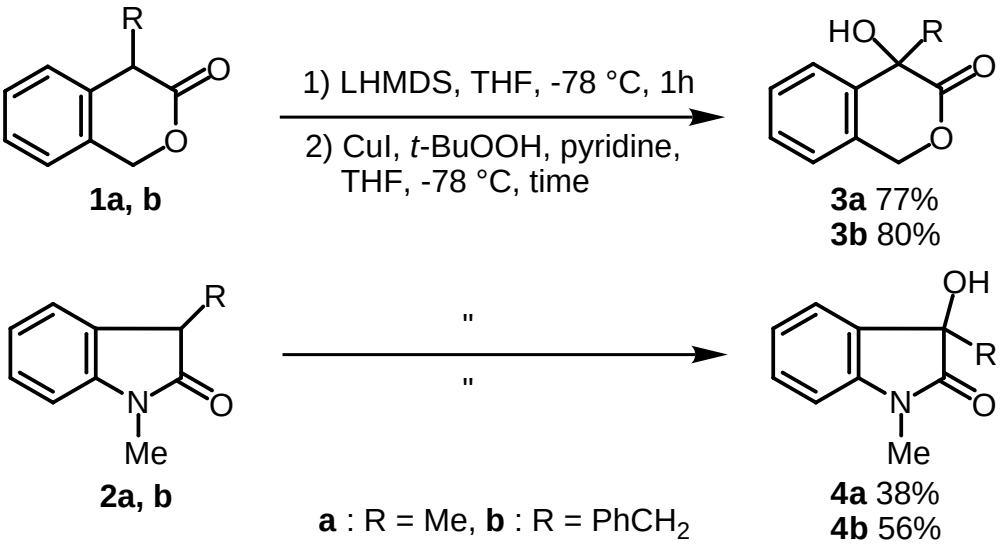


Table 1. CuI-Promoted Hydroxylation onto Lactones (1a,b) and Lactams (2a,b) after Enolization with LHMDS.

Entry	Compd.	*t*-BuOOH (mol eq.)	Pyridine (mol eq.)	Time (h)	Product	Yield (%)
1	**1a**	1.1	4.4	36	**3a**	77
2	**1b**	2.2	4.2	40	**3b**	80
3	**2a**	"	8.8	60	**4a**	38
4	**2b**	"	"	20	**4b**	56

Subsequently, α-hydroxylation of **1a**,**b** and **2a**,**b** was attempted by using KHMDS and NMO, as shown in Scheme 3. Namely, after enolization of **1a**,**b** and **2a**,**b** with KHMDS in THF at -78 °C for 1 h, each resultant potassium enolate in THF was allowed to react with a mixture of CuI, NMO, and pyridine in THF at each indicated temperature. The desired oxidative hydroxylation proceeded to furnish the corresponding α-hydroxy lactones (**3a**,**b**) and α-hydroxy lactams (**4a**,**b**) in 47-70% yields, respectively, as shown in Table 2. The similar hydroxylation onto the potassium enolate of **1a** without use of CuI turned out to be 68% recovery of **1a** with **3a** in 9% yield. Thus, CuI seems to be essential for this hydroxylation in the presence of NMO and pyridine. This CuI-promoted α-hydroxylation onto the lactones and lactams using more than 2.2 mol eq. of *t*-BuOOH and NMO resulted in very low yields of their α-hydroxy products together with miscellaneous products.

Scheme 3

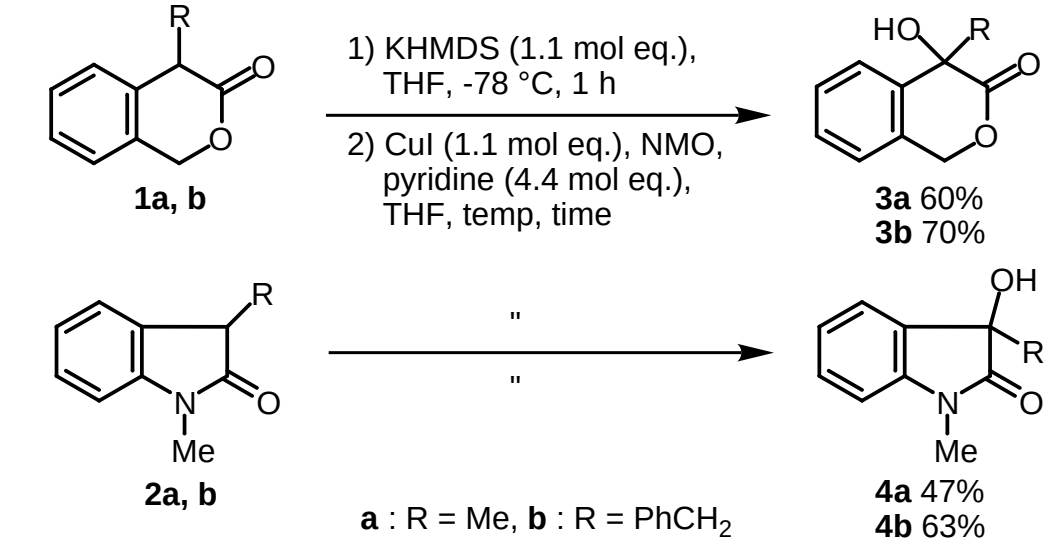
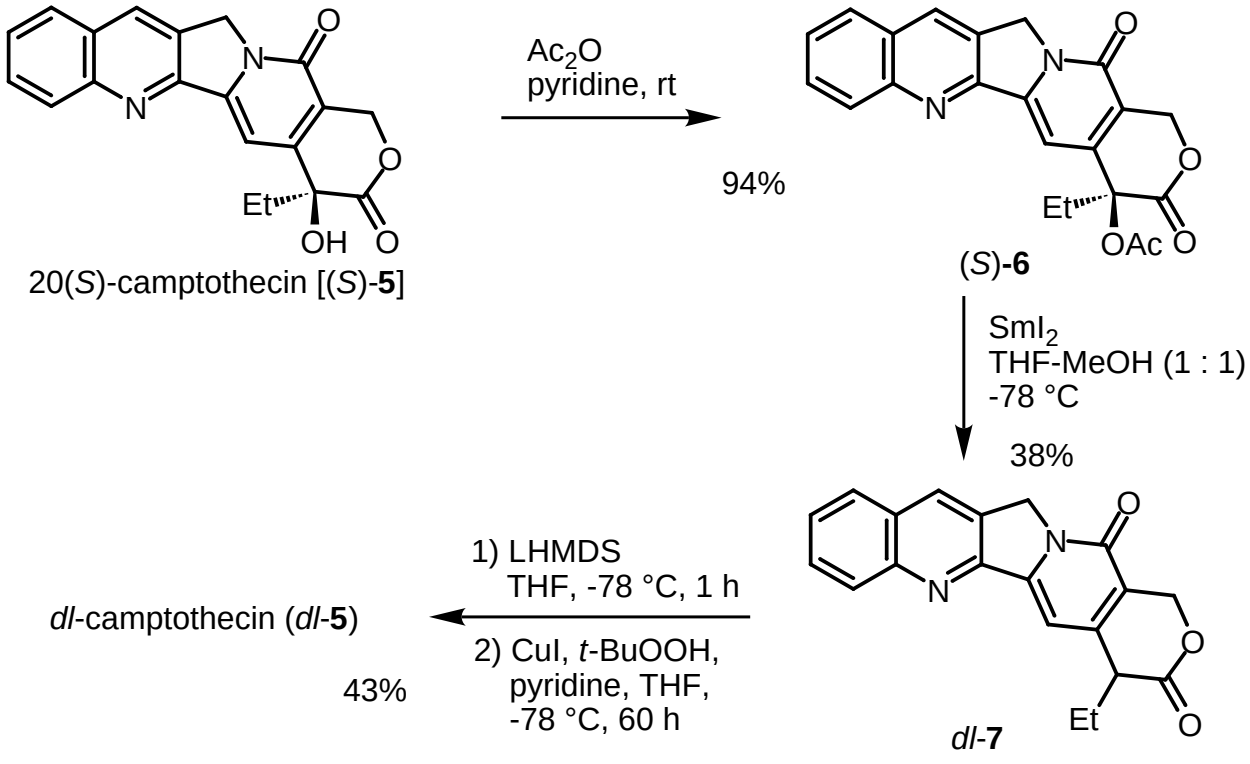


Table 2. CuI-Promoted Hydroxylation onto Lactones (1a,b) and Lactams (2a,b) after Enolization with KHMDS.

Entry	Compd.	NMO (mol eq.)	Temp (°C)	Time (h)	Product	Yield (%)
1	**1a**	1.1	rt	15	**3a**	60
2	**1b**	2.2	-78 and then rt	6 12	**3b**	70
3	**2a**	"	-78 and then rt	6 30	**4a**	47
4	**2b**	"	"	"	**4b**	63

Finally, we applied this CuI-promoted α-hydroxylation to the conversion of *dl*-desoxycamptothecin (*dl*-**7**)[14,17] to *dl*-camptothecin (*dl*-**5**),[14,17,18] as shown in Scheme 4. The compound (*dl*-**7**) was prepared by treatment of 20(*S*)-camptothecin acetate [(*S*)-**6**], obtained by acetylation of 20(*S*)-camptothecin [(*S*)-**5**],[19] with SmI_2 in THF-MeOH (1:1) at -78°C.[20] After enolization of *dl*-**7** with KHMDS in THF at -78 °C, the resultant lithium enolate was treated with

Scheme 4



a mixture of CuI, *t*-BuOOH, and pyridine in THF at -78 °C under argon atmosphere to afford

dl-camptothecin (*dl*-**5**) in 43% yield. Recently, we have accomplished an asymmetric total synthesis of 20(*S*)-camptothecin [(*S*)-**5**], in which *dl*-desoxycamptothecin (*dl*-**7**) was successfully synthesized from a pyrrolidinone derivative.[21] Thus, the conversion of *dl*-**7** to *dl*-**5** exploiting the CuI-promoted hydroxylation method is regarded as a total synthesis of *dl*-camptothecin *(dl*-**5**).

EXPERIMENTAL

All melting points were measured on a Yanagimoto apparatus and are uncorrected. IR spectra were recorded on a JASCO FT/IR-420 infrared Fourier transform spectrophotometer. ^{1}H-NMR (300 MHz) spectra were taken on a JEOL JNM-AL 300 spectrometer with tetramethylsilane as an internal standard, and chemical shifts are recorded in δ values (ppm). HR-MS spectra were measured on a JEOL JMS SX-102A mass spectrometer using a direct inlet system. Elementary combustion analyses were performed by a Yanagimoto CHN Corder. All reactions were monitored by thin-layer chromatography employing 0.25 mm E. Merck silica gel plates (60F-254). Preparative thin-layer chromatography was performed on 0.5 mm E. Merck silica gel (60F-254). Column chromatography was carried out on Kanto silica gel 60N (spherical neutral, 63-210 μm). THF was employed after treating with ketyl radical, distillation, and passing argon for 1 h.

4-Methyl-2-benzopyran-3-one (1a)

To a solution of isochroman-3-one (500 mg, 3.4 mmol) in THF (30 mL) and HMPA (5 mL) was added dropwise *n*-BuLi (1.61 M hexane solution, 2096 μL, 3.4 mmol) at -78 °C under argon, and the mixture was stirred at -78 °C for 1 h. Then, MeI (1350 μL, 16.9 mmol) was added dropwise with stirring, and the whole mixture was stirred at -78 °C for 1 h. The reaction mixture was treated with 5% HCl, extracted with $CHCl_3$, and then the $CHCl_3$ extract was washed with

brine. The organic layer was dried over $MgSO_4$ and filtered, and the filtrate was concentrated *in vacuo*. The oily residue was purified by column chromatography on silica gel with hexane-AcOEt (2 : 1) to give known compound (**1a**)[11] (491.9 mg, 90%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.65 (3H, d, *J* = 7.0 Hz), 3.65 (1H, q, *J* = 7.0 Hz), 5.28 (1H, d, *J* = 13.8 Hz), 5.35 (1H, d, *J* = 13.8 Hz), 7.23-7.42 (4H, m); IR (neat) 1745 cm^{-1}; HR-MS Calcd for $C_{10}H_{10}O_2$: 162.0681, Found *m*/*z*: 162.0691 (M^+).

4-Benzyl-2-benzopyran-3-one (1b)

A solution of *n*-BuLi (1.61 M hexane solution, 1383 μL, 2.2 mmol) was added dropwise to a solution of isochroman-3-one (300 mg, 2.0 mmol) in THF (30 mL) and HMPA (6 mL) at -78 °C under argon. The mixture was stirred at -78 °C for 1 h, and then benzyl bromide (241 μL, 2.0 mmol) was added dropwise with stirring. After being stirred at -78 °C for 1 h, the reaction mixture was treated with 5% HCl, extracted with $CHCl_3$, and then the $CHCl_3$ extract was washed with brine. The organic layer was dried over $MgSO_4$, filtered, and the filtrate was evaporated *in vacuo*. The oily residue was purified by column chromatography on silica gel with hexane-AcOEt (2 : 1) to give compound (**1b**) (242.0 mg, 50%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 3.29 (2H, d, *J* = 6.4 Hz), 4.00 (1H, t, *J* = 6.4 Hz), 4.74 (1H, d, *J* = 14.3 Hz), 5.08 (1H, d, *J* = 14.3 Hz), 6.94-7.28 (9H, m); IR (neat) 1740 cm^{-1}; HR-MS Calcd for $C_{16}H_{14}O_2$: 238.0994, Found *m*/*z*: 238.0987 (M^+); Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.41; H, 6.07.

1,3-Dimethylindolin-2-one (2a)

To a solution of 1-methylindolin-2-one (400 mg, 2.7 mmol) in THF (30 mL) and HMPA (6 mL) was added dropwise a solution of lithium bis(trimethylsilyl)amide (1.08 M hexane solution, 2516 μL, 2.7 mmol) at -78 °C under argon. The mixture was stirred at -78 °C for 1 h, and then MeI (2531 μL, 4.1 mmol) was added dropwise with stirring. After being stirred at -78 °C for 1 h, the reaction mixture was submitted to the usual work-up to give an oily residue.

Chromatographic purification of the residue on a silica gel column with hexane-AcOEt (2 : 1) afforded compound (**2 a**) (184 mg, 42%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.48 (3H, d, *J* = 7.7 Hz), 3.21 (3H, s), 3.43 (1H, q, *J* = 7.7 Hz), 6.82 (1H, d, *J* = 7.7 Hz), 7.06 (1H, dd, *J* = 7.7 and 7.3 Hz), 7.22-7.30 (2H, m); IR (neat) 1710 cm^{-1}; HR-MS Calcd for $C_{10}H_{11}NO$: 160.0762, Found *m*/*z*: 160.0751 (M^+).

3-Benzyl-1-methylindolin-2-one (2b)

To a solution of 1-methylindolin-2-one (500 mg, 3.4 mmol) in THF (30 mL) and HMPA (6 mL) was added dropwise a solution of lithium bis(trimethylsilyl)amide (1.08 M hexane solution, 3146 μL, 3.4 mmol) at -78 °C under argon. The mixture was stirred at -78 °C for 1 h, and then benzyl bromide (606 μL, 5.1 mmol) was added dropwise with stirring. After being stirred at -78 °C for 1 h, the reaction mixture was submitted to the usual work-up to give a purple residue. The residue was purified by chromatography on a silica gel column with hexane-AcOEt (2 : 1) to afford compound (**2 b**) (456.3 mg, 53%) as a purple solid. mp 61-62 °C; ^{1}H NMR ($CDCl_3$) δ 2.87 (1H, dd, *J* = 13.6 and 9.4 Hz), 3.16 (3H, s), 3.50 (1H, dd, *J* = 13.6 and 4.4 Hz), 3.71 (1H, dd, *J* = 9.4 and 4.4 Hz), 6.72-6.76 (2H, m), 6.91 (1H, dd, *J* = 7.9 and 7.2 Hz), 7.15-7.28 (6H, m); IR (KBr) 1698 cm^{-1}; HR-MS Calcd for $C_{16}H_{15}NO$: 237.1154, Found *m*/*z*: 237.1171 (M^+).

General Procedure for Copper(I) Iodide-Promoted Hydroxylation Using *t*-BuOOH and Pyridine

4-Hydroxy-4-methyl-2-benzopyran-3-one (3a)

4-Methyl-2-benzopyran-3-one (**1a**) (50 mg, 0.31 mmol) was dissolved in THF (10 mL) degassed with argon, and then a solution of lithium hexamethyldisilazide (1.08 M hexane solution, 315 μL, 0.34 mmol) was added dropwise at -78 °C under argon atmosphere. After being stirred at -78 °C for 1 h, the resultant solution was employed as the lithium enolate of **1a**. Pyridine (109 μL, 1.36 mmol) and *tert*-butyl hydroperoxide (37 μL, 0.34 mmol) were added to a

suspension of copper(I) iodide (64.6 mg, 0.34 mmol) in THF (10 mL) degassed with argon in another vessel, and the mixture was stirred at -78 °C for 1 h under argon atmosphere. To the resultant suspension was added a solution of the lithium enolate of **1a** by using a cannula system, and then the whole mixture was stirred at -78 °C for 36 h under argon. The reaction mixture was treated with 5% HCl, 20% Na_2SO_3, and extracted with $CHCl_3$. The $CHCl_3$ extract was submitted to the usual work-up to give an oily residue. The residue was chromatographed on a silica gel plate with hexane-AcOEt (2 : 1) to give compound (**3a**) (42.5 mg, 77%) as a white solid. mp 68-70 °C; ^{1}H NMR ($CDCl_3$) δ 1.61 (3H, s), 3.68 (1H, s), 5.34 (1H, d, *J* = 14.5 Hz), 5.53 (1H, d, *J* = 14.5 Hz), 7.18 (1H, d, *J* = 7.5 Hz), 7.35 (1H, dd, *J* = 7.5 and 7.5 Hz), 7.45 (1H, dd, *J* = 7.5 and 7.5 Hz), 7.70 (1H, d, *J* = 7.5 Hz); IR (KBr) 3490, 1735 cm^{-1}; HR-MS Calcd for $C_{10}H_{10}O_3$: 178.0630, Found *m/z*: 178.0642 (M^+); Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.22; H, 5.67.

4-Benzyl-4-hydroxy-2-benzopyran-3-one (3b)

The reaction was carried out by employing **1b** (30 mg, 0.13 mmol), lithium hexamethyldisilazide (1.08 M hexane solution, 128.2 μL, 0.14 mmol), pyridine (44.8 mL, 0.55 mmol), *tert*-butyl hydroperoxide (34.7 μL, 0.28 mmol), and copper(I) iodide (26.4 mg, 0.14 mmol) to give compound (**3b**) (25.5 mg, 80%) as colorless needles from benzene. mp 130-131 °C; ^{1}H NMR ($CDCl_3$) δ 3.12 (2H, s), 3.70 (1H, s), 5.00 (1H, d, *J* = 14.7 Hz), 5.22 (1H, d, *J* = 14.7 Hz), 6.95-6.97 (2H, m), 7.10 (1H, d, *J* = 7.2 Hz), 7.18-7.31 (3H, m), 7.31-7.41 (2H, m), 7.53 (1H, d, *J* = 5.5 Hz); IR (KBr) 3447, 1725 cm^{-1}; HR-MS Calcd for $C_{16}H_{14}O_3$: 254.0943, Found *m/z*: 254.0935 (M^+); Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.39; H, 5.59.

1,3-Dimethyl-3-hydroxyindolin-2-one (4a)

The reaction was carried out by employing **2a** (14 mg, 0.087 mmol), lithium hexamethyldisilazide (1.08 M hexane solution, 88.5 μL, 0.096 mmol), pyridine (61.8 μL, 0.764 mmol), *tert*-butyl hydroperoxide (23.9 μL, 0.19 mmol), and copper(I) iodide (18.2 mg, 0.096

mmol) to give compound (**4a**) (5.9 mg, 38%) as colorless prisms from benzene. mp 146-147 °C; ^{1}H NMR ($CDCl_3$) δ 1.61 (3H, s), 3.16 (1H, br s), 3.20 (3H, s), 6.85 (1H, d, *J* = 7.9 Hz), 7.11 (1H, dd, *J* = 7.7 and 7.3 Hz), 7.33 (1H, dd, *J* = 7.9 and 7.7 Hz), 7.41 (1H, d, *J* = 7.3 Hz); IR (KBr) 3306, 1698 cm^{-1}; HR-MS Calcd for $C_{10}H_{11}NO_2$: 177.0790, Found *m/z*: 177.0797 (M^+); Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.81; H, 6.29; N, 7.79.

3-Benzyl-3-hydroxy-1-methyl-indolin-2-one (4b)

The reaction was carried out by employing **2b** (30 mg, 0.126 mmol), lithium hexamethyldisilazide (1.08 M hexane solution, 128.8 μL, 0.139 mmol), pyridine (90 μL, 1.113 mmol), *tert*-butyl hydroperoxide (34.8 μL, 0.278 mmol), and copper(I) iodide (26.5 mg, 0.139 mmol) to give compound (**4b**) (18 mg, 56%) as pale yellow prisms from benzene. mp 161-162 °C;^{1}H NMR ($CDCl_3$) d 2.77 (1H, s), 3.01 (3H, s), 3.12 (1H, d, *J* = 12.9 Hz), 3.30 (1H, d, *J* = 12.9 Hz), 6.65 (1H, d, *J* = 7.9 Hz), 6.94-7.28 (8H, m); IR (KBr) 3382, 1700 cm^{-1}; HR-MS Calcd for $C_{16}H_{15}NO_2$: 253.1103, Found *m/z*: 253.1095 (M^+); Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.85; H, 5.97; N, 5.53. Found: C, 75.51; H, 5.97; N, 5.53.

General Procedure for Copper(I) Iodide-Promoted Hydroxylation Using *N*-Methylmorpholine *N*-Oxide and Pyridine

4-Hydroxy-4-methyl-2-benzopyran-3-one (3a)

To a solution of 4-methyl-2-benzopyran-3-one (**1a**) (50 mg, 0.31 mmol) in THF (10 mL) degassed with argon was added dropwise potassium hexamethyldisilazide (1.08 M toluene solution, 564 μL, 0.34 mmol) at -78 °C under argon atmosphere. After being stirred at -78 °C for 1 h, the resultant solution was employed as the potassium enolate of **1a**. Pyridine (109 μL, 1.36 mmol) and *N*-methylmorpholine *N*-oxide (40.9 mg, 0.34 mmol) were added to a suspension of copper(I) iodide (64.6 mg, 0.34 mmol) in THF (10 mL) degassed with argon in another vessel, and the mixture was stirred at -78 °C for 1 h under argon atmosphere. To the resultant suspension was added a solution of the potassium enolate of **1a** by using a cannula

system at -78 °C, and then the whole mixture was stirred at room temperature for 15 h. The reaction mixture was treated as usual to give compound (**3a**) (33.2 mg, 60%).

Other compounds (**1b**, **2a**, and **2b**) were also submitted to the similar treatment described above to furnish the corresponding hydroxy products [**3b** (70% yield), **4a** (47% yield), and **4b** (63% yield)], respectively (See Table 2).

20(*S*)-Camptothecin Acetate [(*S*)-6]

To a suspension of 20(*S*)-camptothecin [(*S*)-**5**] (500 mg, 1.44 mmol) in pyridine (40 mL) was added acetic anhydride (2031 μL, 21.54 mmol) at 0 °C. After being stirred at rt for 3 days, the reaction mixture was evaporated *in vacuo* to give an oily residue, which was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with brine, dried over $MgSO_4$, and filtered. After evaporation of the filtrate *in vacuo*, the residue was crystallized in $CHCl_3$-MeOH to afford 20(*S*)-camptothecin acetate [(*S*)-**6**] (528.5 mg, 94%) as colorless needles. mp 287-290 °C decomp (lit.,[19] 271-274 °C decomp);^{1}H NMR ($CDCl_3$) δ 0.98 (3H, t, *J* = 7.5 Hz), 2.09-2.33 (2H, m), 2.22 (3H, s), 5.29 (2H, s), 5.42 (1H, d, *J* = 17.3 Hz), 5.68 (1H, d, *J* = 17.3 Hz), 7.23 (1H, s), 7.68 (1H, dd, *J* = 8.5 and 7.2 Hz), 7.85 (1H, dd, *J* = 8.3 and 7.2 Hz), 7.95 (1H, d, *J* = 8.3 Hz), 8.23 (1H, d, *J* = 8.5 Hz), 8.40 (1H, s); IR (KBr) 1747, 1670, 1619 cm^{-1}; HR-MS Calcd for $C_{22}H_{18}N_2O_5$: 390.1216, Found *m/z*: 390.1203 (M^+).

dl-Desoxycamptothecin (*dl*-7)

To a suspension of 20(*S*)-camptothecin acetate [(*S*)-**6**] (500 mg, 1.3 mmol) in a degassed solution of MeOH (10 mL) and THF (10 mL) was added dropwise a 0.1M THF solution of SmI_2 (51 mL, 5.1 mmol) with stirring at -78 °C under argon atmosphere. After being stirred at -78 °C for 4 h, the reaction mixture was treated with sat. K_2CO_3 aqueous solution and then acidified with 5% HCl. The acidic solution was extracted with $CHCl_3$, and the $CHCl_3$ extract was dried over $MgSO_4$. After filtration, the filtrate was evaporated *in vacuo* to give a residue. The residue

was purified on a silica gel column with $CHCl_3$-MeOH (50 : 1) to afford *dl*-desoxycamptothecin (*dl*-**7**) (163 mg, 38%) as a pale yellow solid from $CHCl_3$-AcOEt. mp 258-260 °C decomp (lit.,[17a] mp 258-260 °C decomp);^{1}H NMR ($CDCl_3$) δ 1.10 (3H, t, *J* = 7.3 Hz), 2.06-2.16 (2H, m), 3.64 (3H, t, *J* = 6.4 Hz), 5.31 (2H, s), 5.40 (1H, d, *J* = 16.3 Hz), 5.58 (1H, d, *J* = 16.3 Hz), 7.20 (1H, s), 7.68 (1H, dd, *J* = 8.4 and 7.0 Hz), 7.84 (1H, dd, *J* = 7.9 and 7.0 Hz), 7.95 (1H, d, *J* = 7.9 Hz), 8.23 (1H, d, *J* = 8.4 Hz), 8.40 (1H, s); IR (KBr) 1738, 1663, 1603 cm^{-1}; HR-MS Calcd for $C_{22}H_{16}N_2O_3$: 332.1161, Found *m/z*: 332.1176(M^+).

***dl*-Camptothecin (*dl*-5)**

The reaction was carried out by employing *dl*-**7** (20 mg, 0.060 mmol), lithium hexamethyldisilazide (1.08 M hexane solution, 61.3 μL, 0.066 mmol), pyridine (42.2 μL, 0.530 mmol), *tert*-butyl hydroperoxide (16.6 μL, 0.132 mmol), and copper(I) iodide (12.6 mg, 0.066 mmol) to give *dl*-camptothecin (*dl*-**5**) (9 mg, 43%) as pale a yellow solid from MeCN-MeOH. mp 287-288 °C decomp. (lit.,[18] 287-288 °C decomp); ^{1}H NMR [$CDCl_3$-MeOH (4 : 1)] δ 1.05 (3H, t, *J* = 7.3 Hz), 1.90-1.98 (2H, m), 5.32 (2H, s), 5.33 (1H, d, *J* = 16.5 Hz), 5.71 (1H, d, *J* = 16.5 Hz), 7.69 (1H, dd, *J* = 8.5 and 7.5 Hz), 7.75 (1H, s), 7.82 (1H, dd, *J* = 8.1 and 7.5 Hz), 7.97 (1H, d, *J* = 8.1 Hz), 8.23 (1H, d, *J* = 8.5 Hz), 8.47 (1H, s); IR (KBr) 1652, 1602, 1581 cm^{-1}; HR-MS Calcd for $C_{22}H_{16}N_2O_4$: 348.1110, Found *m/z*: 348.1090(M^+).

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