Electronic Supplementary Information: part 1

Photoactivatable HNO-releasing Compounds Using the retro-Diels-Alder Reaction

Yusuke Adachi, Hidehiko Nakagawa*, Kazuya Matsuo, Takayoshi Suzuki, and Naoki Miyata*

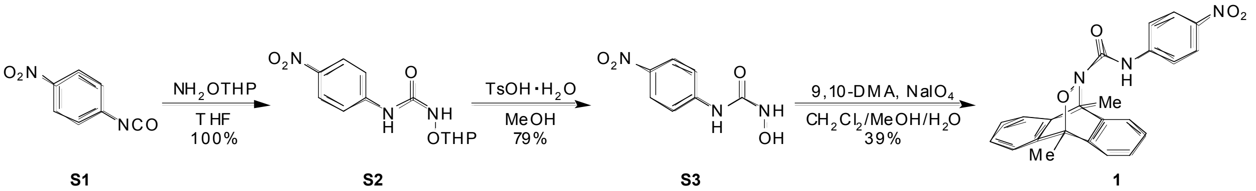
Graduate School of Pharmaceutical Sciences, Nagoya City University, 3-1 Tanabe-dori, Mizuho-ku, Nagoya, Aichi 467-8673, Japan

E-mail: deco@phar.nagoya-cu.ac.jp (H.N.), and miyata-n@phar.nagoya-cu.ac.jp (N.M.)

<Synthesis>

General Methods. Melting points were determined using a Yanaco micro melting point apparatus or a Büchi B-545 melting point apparatus and were left uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra and carbon nuclear magnetic resonance (^{13}C-NMR) spectra were recorded on a JEOL JNM-LA500 or JEOL JNM-A500 spectrometer in solvent as indicated. Chemical shifts (δ) are reported in parts per million (ppm) relative to the internal standard tetramethylsilane (TMS). Elemental analysis was performed with a Yanaco CHN CORDER NT-5 analyzer, and all values were within ±0.4% of the calculated values. UV/vis spectra were measured using an Agilent 8453 spectrometer. IR spectra were recorded on an Avatar360. GC-MS analyses were performed on a Shimadzu GCMS-QP2010. FAB-MS were recorded on a JEOL JMS-SX102A mass spectrometer. Reagents and solvents were purchased from Aldrich, Tokyo Kasei Kogyo, Wako Pure Chemical Industries, and Kanto Kagaku and used without further purification. Flash chromatography was performed using Silica Gel 60 (particle size 0.046–0.063 mm) supplied by Merck.

Scheme S1. Preparation of **1**.



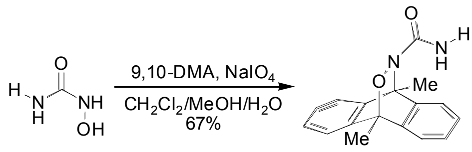
***N*-(Tetrahydropyran-2-yl)oxy-*N’*-(4-nitrophenyl)urea (S2).** To a solution of NH_2OTHP (936 mg, 8 mmol) in dehydrated THF (16 mL) was added **S1** (1313 mg, 8 mmol) dropwise at 0 °C. The reaction mixture was stirred for 40 min at 0 °C. After the solvent was removed, purification by silica gel flash chromatography (AcOEt/*n*-hexane = 2/3) gave 2256 mg (100%) of **S2** as yellow solids: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 8.63 (1H, s), 8.21 (2H, d, J = 9.0 Hz), 7.63 (2H, d, J = 9.0 Hz), 7.33 (1H, s), 4.86 (1H, m), 4.09 (1H, m), 3.66 (1H, m), 1.90 (2H, m), 1.64 (4H, m).

***N*-Hydroxy-*N’*-(4-nitrophenyl)urea (S3).** To a solution of **S2** (1950 mg, 6.9 mmol) in MeOH (150 mL) was added $TsOH \cdot H_2O$ (119 mg, 0.69 mmol). The reaction mixture was stirred for 23 h at room temperature. After the solution was concentrated under reduced pressure, purification by silica gel flash chromatography

(AcOEt/*n*-hexane = 3/1) gave 1068 mg (79%) of **S3** as yellow solids: ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 9.51 (1H, s), 9.29 (1H, s), 9.16 (1H, s), 8.16 (2H, d, J = 9.5 Hz), 7.92 (2H, d, J = 9.5 Hz).

9,10-Dihydro-9,10-dimethyl-*N*-(4-nitrophenyl)-9,10-(epoxyimino)anthracene-11-carboxamide (1). To a suspension of 9,10-DMA (103 mg 0.5 mmol) in CH_2Cl_2 (8.0 mL) and MeOH (1.0 mL) containing $NaIO_4$ (213 mg, 1 mmol) was added a solution of **S3** (197 mg, 1 mmol) in MeOH (8.0 mL) and H_2O (0.8 mL) dropwise at 0 °C. The reaction mixture was stirred for 3 h at 0 °C, and diluted with CH_2Cl_2 and H_2O. Aqueous $Na_2S_2O_3$ was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2. The organic layers were combined with the separated CH_2Cl_2 layer, and then dried over Na_2SO_4. After the solvent was removed, purification by silica gel flash chromatography (AcOEt/*n*-hexane = 1/20 to 1/3) gave 79 mg (39%) of **1** as yellow solids. 28.0 mg of solids was recrystallized from AcOEt/*n*-hexane to give 24.6 mg of pale yellow crystals: mp 138.4–139.2 °C (decomp.); R_f = 0.40 (AcOEt/*n*-hexane = 1/3); UV/vis (CH_3CN): $\varepsilon_{323\,nm}$= 1.73 × 10^4 $M^{-1}cm^{-1}$; IR (KBr): ν = 3368 cm^{-1} (N-H), 1687 cm^{-1} (C=O), 1596 cm^{-1} (N-H), 1506 cm^{-1} (NO_2), 1340 cm^{-1} (NO_2); ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 9.30 (1H, s), 8.08 (2H, d, J = 9.0 Hz), 7.65 (2H, d, J = 9.5 Hz) 7.54 (2H, m), 7.51 (2H, m), 7.31 (4H, m), 2.60 (3H, s), 2.33 (3H, s); ^{13}C-NMR (DMSO-d_6, 500 MHz, δ; ppm) 159.05, 144.85, 141.97, 141.16, 140.23, 127.28, 127.14, 124.37, 121.72, 120.92, 112.34, 79.81, 63.92, 16.86, 14.91; MS (FAB) *m/z*: 402 ([M+H]$^+$); Anal. Calcd. for $C_{23}H_{19}N_3O_4$: C, 68.82; H, 4.77; N, 10.47. Found: C, 68.75; H, 4.86; N, 10.45.

Scheme S2. Preparation of **2**.

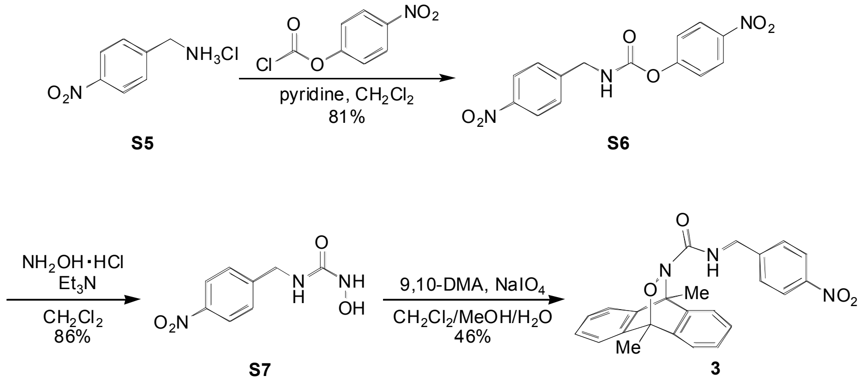


S4

2

9,10-Dihydro-9,10-dimethyl-9,10-(epoxyimino)anthracene-11-carboxamide (2). To a suspension of 9,10-DMA (206 mg, 1 mmol) in CH_2Cl_2 (10 mL) and MeOH (5.0 mL) containing $NaIO_4$ (426 mg, 2 mmol) was added a solution of **S4** (152 mg, 2 mmol) in MeOH (2.0 mL) and H_2O (1.0 mL) dropwise at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, and diluted with CH_2Cl_2 and H_2O. Aqueous $Na_2S_2O_3$ was added to discharge the color of iodine, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2. The organic layers were combined with the separated CH_2Cl_2 layer, and then dried over Na_2SO_4. After the solvent was removed, the resulting residue was purified by silica gel flash chromatography (AcOEt/*n*-hexane = 1/1) and recrystallized from AcOEt/*n*-hexane to give 65 mg (23%) of **2** as white crystals: mp 183.1–184.1 °C (decomp.); R_f = 0.29 (AcOEt/*n*-hexane = 1/1); UV/vis (CH_3CN): $\varepsilon_{260\,nm}$= 3.60 × 10^3 $M^{-1}cm^{-1}$; IR (KBr): ν = 3522 cm^{-1} (N-H), 3397 cm^{-1} (N-H), 1678 cm^{-1} (C=O), 1545 cm^{-1} (N-H); ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.50 (2H, d, J = 7.0 Hz), 7.37 (2H, d, J = 7.5 Hz), 7.28 (4H, m), 2.67 (3H, s), 2.25 (3H, s); ^{13}C-NMR (DMSO-d_6, 500 MHz, δ; ppm) 162.99, 141.48, 140.45, 126.86, 126.68, 121.39, 120.51, 78.18, 63.07, 16.99, 14.67; MS (EI) *m/z*: 206 (-$NOCONH_2$); MS (FAB) *m/z*: 281 ([M+H]$^+$); Anal. Calcd. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 73.01; H, 5.51; N, 9.89.

Scheme S3. Preparation of **3**.

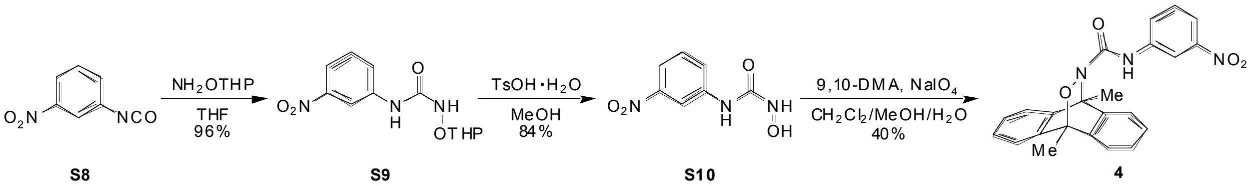


4-Nitrophenyl *N*-(4-nitrobenzyl)carbamate (S6). To a suspension of **S5** (565 mg, 3 mmol) and pyridine (711 mg, 9 mmol) in dehydrated CH_2Cl_2 (10 mL) was added 4-nitrophenyl chloroforamte (604 mg, 3 mmol) at 0 °C. The reaction mixture was stirred for 90 min at room temperature. The mixture was washed with 1 N HCl and H_2O. Then the organic layer was dried over Na_2SO_4 and concentrated to give 773 mg (81%) of **S6** as white solids: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 8.26 (4H, m), 7.54 (2H, d, $J = 8.5$ Hz), 7.35 (2H, d, $J = 9.0$ Hz), 5.59 (1H, s), 4.59 (2H, d, $J = 6.0$ Hz).

***N*-Hydroxy-*N*'-(4-nitrobenzyl)urea (S7).** To a suspension of $NH_2OH·HCl$ (2084 mg, 30 mmol) and Et_3N (10.4 mL, 75 mmol) in CH_2Cl_2 (70 mL) was added **S6** (951 mg, 3 mmol) dropwise. The reaction mixture was stirred for 160 min at room temperature. After filtration, the solvent was removed. Purification by silica gel flash chromatography (AcOEt/*n*-hexane = 8/1) gave 545 mg (86%) of **S7** as white solids: ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 8.70 (1H, s), 8.52 (1H, s), 8.20 (2H, d, $J = 8.5$ Hz), 7.52 (2H, d, $J = 9.0$ Hz), 7.50 (1H, s), 4.36 (2H, d, $J = 6.0$ Hz).

9,10-Dihydro-9,10-dimethyl-*N*-(4-nitrobenzyl)-9,10-(epoxyimino)anthracene-11-carboxamide (3). To a suspension of 9,10-DMA (103 mg, 0.5 mmol) in CH_2Cl_2 (4.0 mL) and MeOH (1.0 mL) containing $NaIO_4$ (213 mg, 1.0 mmol) was added a suspension of **S7** (211 mg, 1.0 mmol) in MeOH (6.0 mL) and H_2O (0.5 mL) dropwise at 0 °C. The reaction mixture was stirred for 90 min at 0 °C, and diluted with CH_2Cl_2 and H_2O. Aqueous $Na_2S_2O_3$ was added to the mixture, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2. The organic layer was combined with separated CH_2Cl_2 layer, and then dried over Na_2SO_4. After the solvent was removed, purification by silica gel flash chromatography (AcOEt/*n*-hexane = 1/10 to 1/2) gave 96 mg (46%) of **3** as white solids. 81.7 mg of solids was recrystallized from AcOEt to give 33.0 mg of white crystals: mp 128.8–129.4 °C (decomp.); $R_f = 0.23$ (AcOEt/*n*-hexane = 1/2); UV/vis (CH_3CN): $\varepsilon_{277\,\mathrm{nm}} = 1.05 \times 10^4$ $M^{-1}cm^{-1}$; IR (KBr): $\nu = 3446$ cm^{-1} (N-H), 1686 cm^{-1} (C=O), 1488 cm^{-1} (NO_2), 1460 cm^{-1} (CH_2), 1340 cm^{-1} (NO_2); ^{1}H-NMR (DMSO-$d_{6,}$ 500 MHz, δ; ppm) 7.93 (2H, d, $J = 9.0$ Hz), 7.65 (1H, t, $J = 6.0$ Hz), 7.49 (4H, m), 7.36 (4H, m), 6.59 (2H, d, $J = 8.5$ Hz), 4.11 (2H, d, $J = 6.5$ Hz), 2.51 (3H, overlap), 2.27 (3H, s); ^{13}C-NMR (DMSO-$d_{6,}$ 500 MHz, δ; ppm) 162.05, 148.03, 145.92, 141.42, 140.26, 127.15, 126.99, 126.70, 122.86, 121.70, 120.81, 78.65, 63.85, 42.20, 16.97, 14.81; MS (FAB) *m/z*: 416 ($[M+H]^+$); Anal. Calcd. for $C_{24}H_{21}N_3O_4$: C, 69.39; H, 5.10; N, 10.11. Found: C, 69.10; H, 5.22; N, 10.00.

Scheme S4. Preparation of **4**.

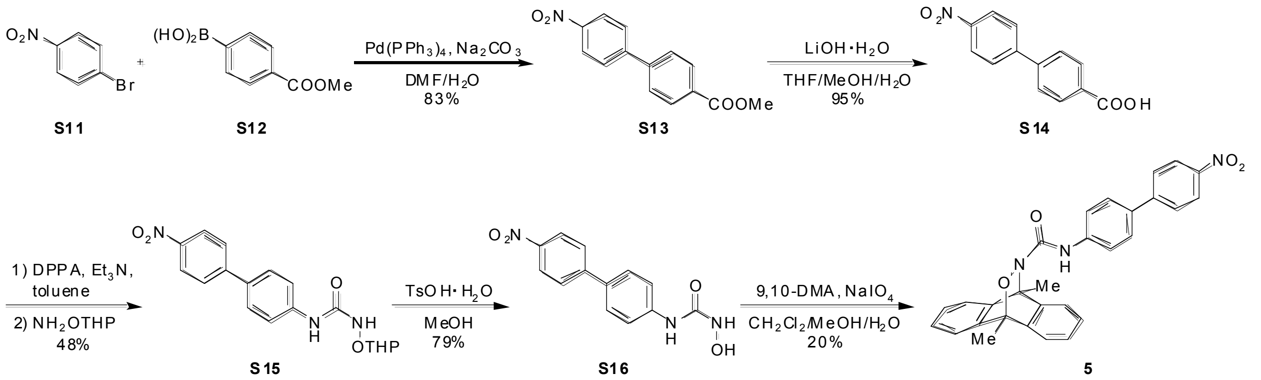


***N*-(Tetrahydropyran-2-yl)oxy-*N'*-(3-nitrophenyl)urea (S9).** To a solution of NH$_2$OTHP (468 mg, 4 mmol) in dehydrated THF (8.0 mL) was added **S8** (657 mg, 4 mmol) dropwise at 0 °C. The reaction mixture was stirred for 55 min at 0 °C. After the solvent was removed, purification by silica gel flash chromatography (AcOEt/*n*-hexane = 1/1) gave 1075 mg (96%) of **S9** as yellow solids: ^{1}H-NMR (CDCl$_3$, 500 MHz, δ; ppm) 8.45 (1H, s), 8.26 (1H, t, J = 2.0 Hz), 7.93 (2H, d, J = 8.5 Hz), 7.48 (1H, t, J = 8.0 Hz), 7.39 (1H, s), 4.87 (1H, m), 4.10 (1H, m), 3.65 (1H, m), 1.91 (2H, m), 1.65 (4H, m).

***N*-Hydroxy-*N'*-(3-nitrophenyl)urea (S10).** To a solution of **S9** (3630 mg, 12.9 mmol) in MeOH (500 mL) was added TsOH·H$_2$O (2236 mg, 1.3 mmol). The reaction mixture was stirred for 24 h at room temperature. After the solution was concentrated under reduced pressure, purification by silica gel flash chromatography (AcOEt/*n*-hexane = 5/2) gave 2146 mg (84%) of **S10** as pale yellow solids: ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 9.38 (1H, s), 9.14 (1H, s), 9.11 (1H, s), 8.70 (1H, t, J = 2.0 Hz), 8.04 (1H, d, J = 8.5 Hz), 7.82 (1H, d, J = 8.5 Hz), 7.53 (1H, t, J = 8.0 Hz).

9,10-Dihydro-9,10-dimethyl-*N*-(3-nitrophenyl)-9,10-(epoxyimino)anthracene-11-carboxamide (4). To a suspension of 9,10-DMA (618 mg 3 mmol) in CH$_2$Cl$_2$ (35 mL) and MeOH (15 mL) containing NaIO$_4$ (1600 mg, 7.5 mmol) was added a solution of **S10** (1180 mg, 6 mmol) in MeOH (30 mL) and H$_2$O (4.0 mL) dropwise at 0 °C. The reaction mixture was stirred for 30 min at 0 °C, and diluted with CH$_2$Cl$_2$ and H$_2$O. Aqueous Na$_2$S$_2$O$_3$ was added and the layers were separated. The aqueous layer was extracted with CH$_2$Cl$_2$. The organic layers were combined with the separated CH$_2$Cl$_2$ layer, and then dried over Na$_2$SO$_4$. After the solvent was removed, purification by silica gel flash chromatography (*n*-hexane only to AcOEt/*n*-hexane = 1/3) gave 486 mg (40%) of **4** as pale yellow solids. 58.0 mg of solids was recrystallized from AcOEt to give 17.1 mg of white crystals: mp 124.2–125.7 °C (decomp.); R_f = 0.25 (AcOEt/*n*-hexane = 1/3); UV/vis (CH$_3$CN): $\varepsilon_{244\mathrm{nm}} = 4.77 \times 10^4$ M^{-1}cm^{-1}; IR (KBr): ν = 3385 cm^{-1} (N-H), 1691 cm^{-1} (C=O), 1527 cm^{-1} (N-H), 1567 cm^{-1} (NO$_2$), 1342 cm^{-1} (NO$_2$); ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 9.18 (1H, s), 8.34 (1H, m), 7.79 (2H, m), 7.54 (2H, m), 7.51 (2H, m), 7.47 (1H, t, J = 8.5 Hz), 7.31 (4H, m), 2.61 (3H, s), 2.34 (3H, s); ^{13}C-NMR (DMSO-d_6, 500 MHz, δ; ppm) 159.51, 147.71, 141.27, 140.30, 139.70, 129.63, 127.33, 127.19, 126.44, 121.76, 120.96, 117.64, 114.40, 79.72, 63.99, 17.00, 14.97; MS (FAB) *m/z*: 402 ([M+H]$^+$); Anal. Calcd. for C$_{23}$H$_{19}$N$_3$O$_4$: C, 68.82; H, 4.77; N, 10.47. Found: C, 68.46; H, 4.96; N, 10.47.

Scheme S5. Preparation of **5**.



Methyl 4-(4-nitrophenyl)benzenecarboxylate (S13). A mixture of **S11** (606 mg, 3 mmol), **S12** (810 mg, 4.5 mmol), $Pd(PPh_3)_4$ (173 mg, 0.15 mmol), and Na_2CO_3 (636 mg, 6 mmol) in DMF (15 mL) and H_2O (3.0 mL) was stirred for 19 h at 55 °C. The reaction mixture was diluted with H_2O and extracted with AcOEt. After filtration by Celite, the organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification by silica gel flash chromatography (toluene/$CHCl_3$ = 3/1) gave 641 mg (83%) of **S13** as white solids: ^{1}H-NMR ($CDCl_3$, 500MHz, δ; ppm) 8.33 (2H, d, *J* = 9.0 Hz), 8.16 (2H, d, *J* = 8.5 Hz), 7.78 (2H, d, *J* = 9.0 Hz), 7.70 (2H, d, *J* = 9.0 Hz), 3.97 (3H, s).

4-(4-Nitrophenyl)benzenecarboxylic acid (S14). To a solution of **S13** (500 mg, 1.95 mmol) in THF (100 mL) and MeOH (6.0 mL) was added a solution of $LiOH{\cdot}H_2O$ (408 mg, 9.73 mmol) in H_2O (10 mL). The reaction mixture was stirred for 22 h at room temperature. The mixture was diluted with H_2O and washed with ether. The aqueous layer was acidified by 2 N HCl and the resulting precipitation was collected by vacuum filtration to give 451 mg (95%) of **S14** as white solids: ^{1}H-NMR (DMSO-d_6, 500MHz, δ; ppm) 8.34 (2H, d, *J* = 9.0 Hz), 8.08 (2H, d, *J* = 8.0 Hz), 8.04 (2H, d, *J* = 8.5 Hz), 7.93 (2H, d, *J* = 8.5 Hz).

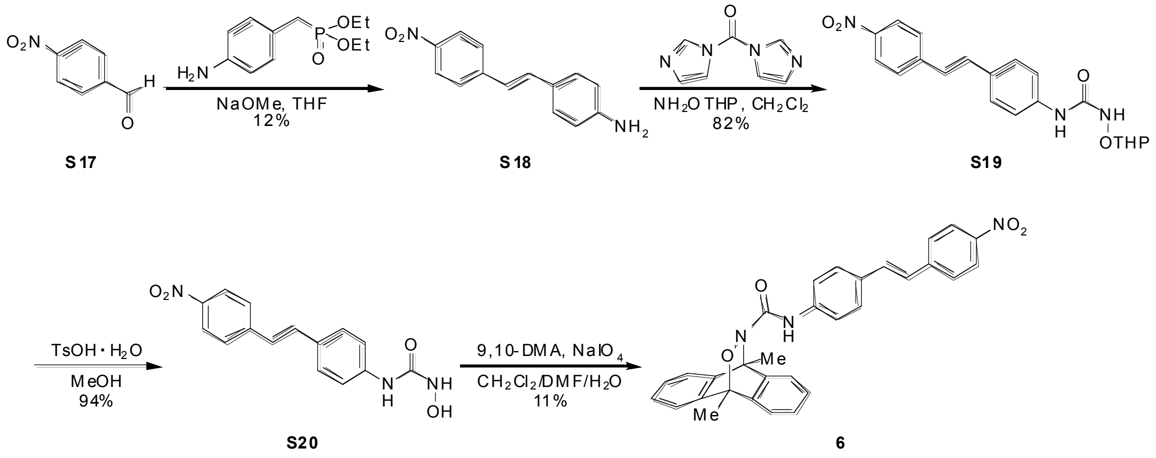
***N*-(Tetrahydropyran-2-yl)oxy-*N'*-4-(4-nitrophenyl)phenylurea (S15).** A solution of **S14** (448 mg, 1.84 mmol), diphenylphosphorylazide (608 mg, 2.21 mmol), and Et_3N (0.306 mL, 2.21 mmol) in dehydrated toluene (58 mL) was heated to 116 °C and stirred for 20 min. Subsequently, a solution of NH_2OTHP (216 mg, 1.84 mmol) in dehydrated toluene (2 mL) was added, and the resulting mixture was further stirred for 2 h at 116 °C. After the solvent was removed, the resulting residue was taken up in $CHCl_3$. The $CHCl_3$ layer was washed with H_2O and brine, dried over Na_2SO_4, and concentrated. Purification by silica gel flash chromatography (toluene/$CHCl_3$/AcOEt = 1/2/1) gave 469 mg of orange solids. 467 mg of solids was recrystallized from AcOEt to give 317 mg (48%) of **S15** as yellow crystals: ^{1}H-NMR ($CDCl_3$, 500MHz, δ; ppm) 8.29 (3H, m), 7.72 (2H, d, *J* = 9.0 Hz), 7.61 (4H, m), 7.28 (1H, s), 4.89 (1H, m), 4.08 (1H, m), 3.66 (1H, m), 1.90 (2H, m), 1.66 (4H, m).

***N*-Hydroxy-*N'*-4-(4-nitrophenyl)phenylurea (S16).** To a solution of **S15** (315 mg, 0.882 mmol) in MeOH (140 mL) was added $TsOH{\cdot}H_2O$ (30 mg, 0.176 mmol). The reaction mixture was stirred for 24 h at room temperature. After removal of the solvent, to the resulting residue was added CH_2Cl_2. The precipitation was washed with CH_2Cl_2 to give 189 mg (79%) of **S16** as pale yellow solids: ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 9.04 (1H, s), 9.03 (1H, s), 8.98 (1H, s), 8.28 (2H, d, *J* = 9.0 Hz), 7.94 (2H, d, *J* = 9.0 Hz), 7.82 (2H, d, *J* =

9.0 Hz), 7.62 (2H, d, *J* = 9.0 Hz).

9,10-Dihydro-9,10-dimethyl-*N*-[4-(4-nitrophenyl)phenyl]-9,10-(epoxyimino)anthracene-11-carboxamide (5). To a suspension of 9,10-DMA (30 mg, 0.144 mmol) in CH_2Cl_2 (2.0 mL) and MeOH (1.0 mL) containing $NaIO_4$ (61 mg, 0.288 mmol) was added a solution of **S16** (79 mg, 0.288 mmol) in MeOH (12 mL) and H_2O (1.0 mL) dropwise at 0 °C. The reaction mixture was stirred for 2 h at 0 °C, and diluted with CH_2Cl_2 and H_2O. Aqueous $Na_2S_2O_3$ was added to the mixture, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2. The organic layers were combined with separated CH_2Cl_2 layer, and then dried over Na_2SO_4. After the solvent was removed, purification by silica gel flash chromatography (AcOEt/*n*-hexane = 1/20 to 1/3) and recrystallization from AcOEt/*n*-hexane gave 14 mg (20%) of **5** as pale yellow crystals: mp 153.2–154.5 °C (decomp.); R_f = 0.37 (AcOEt/*n*-hexane = 1/3); IR (KBr): ν = 3402 cm^{-1} (N-H), 1684 cm^{-1} (C=O), 1594 cm^{-1} (N-H), 1511 cm^{-1} (NO_2), 1338 cm^{-1} (NO_2); ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 8.86 (1H, s), 8.26 (2H, d, *J* = 9.0 Hz), 7.89 (2H, d, *J* = 9.0 Hz), 7.65 (2H, d, *J* = 9.0 Hz), 7.52 (4H, m), 7.48 (2H, d, *J* = 9.0 Hz), 7.31 (4H, m), 2.60 (3H, s), 2.34 (3H, s) ; ^{13}C-NMR (DMSO-d_6, 600 MHz, δ; ppm) 159.35, 146.05, 145.99, 141.18, 140.20, 139.23, 132.03, 127.15, 127.01, 126.98, 123.98, 121.64, 120.77, 120.57, 118.49, 79.35, 63.82, 16.94, 14.88; MS (FAB) *m/z*: 478 ($[M+H]^+$); Anal. Calcd. for $C_{29}H_{23}N_3O_4\cdot 1/2H_2O$: C, 71.59; H, 4.97; N, 8.64. Found: C, 71.41; H, 5.03; N, 8.62.

Scheme S6. Preparation of **6**.



4-[(*1E*)-2-(4-Nitrophenyl)ethenyl]phenylamine (S18). To a suspension of NaH (773 mg, 32.2 mmol) in dehydrated THF (20 mL) was added a solution of diethyl (4-aminobenzyl)phosphonate (2238 mg, 9.2 mmol) in dehydrated THF (20 mL) at 0 °C. The reaction mixture was stirred for 70 min at 0 °C. A solution of **S17** (1390 mg, 9.2 mmol) in dehydrated THF (20 mL) was added. The resulting mixture was further stirred for 2 h at room temperature. The mixture was diluted with H_2O and the whole was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. Purification by silica gel flash chromatography (toluene/$CHCl_3$/AcOEt = 2/4/0.1) gave 258 mg (12%) of **S18** as red-brown solids: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 8.19 (2H, d, *J* = 9.0 Hz), 7.57 (2H, d, *J* = 8.5 Hz), 7.38 (2H, d, *J* = 8.5 Hz), 7.19 (1H, d, *J* = 16.5 Hz), 6.94 (1H, d, *J* = 16.5 Hz), 6.69 (2H, d, *J* = 8.5 Hz).

***N*-(Tetrahydropyran-2-yl)oxy-*N*'-{4-[(*1E*)-2-(4-nitrophenyl)ethenyl]phenyl}urea (S19).** To a solution of NH_2OTHP (176 mg, 1.5 mmol) in dehydrated CH_2Cl_2 (2.0 mL) was added a solution of carbonyl diimidazole (269 mg, 1.66 mmol) in dehydrated CH_2Cl_2 (5.0 mL). The reaction mixture was stirred for 21 h at room temperature. A suspension of **S18** (289 mg, 1.2 mmol) in dehydrated CH_2Cl_2 (12 mL) was added. The resulting mixture was stirred for 29 h at room temperature. The solvent was removed under reduced pressure, and purification by silica gel flash chromatography (AcOEt/*n*-hexane = 2/3) gave 378 mg (82%) of **S19** as light yellow solids: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 8.22 (1H, s), 8.21 (2H, d, J = 9.0 Hz), 7.62 (2H, d, J = 9.0 Hz), 7.52 (4H, s), 7.23 (1H, d, J = 16.5 Hz), 7.07 (1H, d, J = 16.5 Hz), 4.88 (1H, m), 4.07 (1H, m), 3.66 (1H, m), 1.92–1.87 (2H, m), 1.69–1.62 (4H, m).

***N*-Hydroxy-*N*'-{4-[(*1E*)-2-(4-nitrophenyl)ethenyl]phenyl}urea (S20).** To a solution of **S19** (470 mg, 1.23 mmol) in MeOH (150 mL) was added $TsOH \cdot H_2O$ (21 mg, 0.123 mmol). The reaction mixture was stirred for 40 h at room temperature. After removal of the solvent, to the resulting residue was added CH_2Cl_2. The precipitation was collected by vacuum filtration to give 347 mg (94%) of **S20** as yellow solids: ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 9.00 (1H, s), 8.93 (1H, s), 8.93 (1H, s), 8.22 (2H, d, J = 8.5 Hz), 7.83 (2H, d, J = 8.5 Hz), 7.70 (2H, d, J = 9.0 Hz), 7.58 (2H, d, J = 8.5 Hz), 7.47 (1H, d, J = 16.5 Hz), 7.29 (1H, d, J = 16.5 Hz).

9,10-Dihydro-9,10-dimethyl-*N*-{4-[(*1E*)-2-(4-nitrophenyl)ethenyl]phenyl}-9,10-(epoxyimino)anthracene-11-carboxamide (6). To a suspension of 9,10-DMA (45.9 mg, 0.223 mmol) in CH_2Cl_2 (4.0 mL) and DMF (0.5 mL) containing $NaIO_4$ (94.8 mg, 0.445 mmol) was added a solution of **S20** (133.0 mg, 0.445 mmol) in DMF (6.5 mL) and H_2O (0.5 mL) dropwise at 0 °C. The reaction mixture was stirred for 2 h at 0 °C, and diluted with CH_2Cl_2 and H_2O. Aqueous $Na_2S_2O_3$ was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2. The organic layers were combined with separated CH_2Cl_2 layer, and then dried over Na_2SO_4. After the solvent was removed, the resulting residue was purified by silica gel flash chromatography (AcOEt/*n*-hexane = 1/20 to 2/5) and washed with *n*-hexane to give 12.8 mg (11%) of **6** as yellow crystals: mp 140.0–141.2 °C (decomp.); R_f = 0.49 (AcOEt/*n*-hexane = 1/2); IR (KBr): ν = 3403 cm^{-1} (N-H), 1686 cm^{-1} (C=O), 1588 cm^{-1} (N-H), 1517 cm^{-1} (NO_2), 1335 cm^{-1} (NO_2); ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 8.77 (1H, s), 8.21 (2H, d, J = 9.0 Hz), 7,81 (2H, d, J = 9.0 Hz), 7.540-7.491 (6H, m), 7.43 (1H, d, J = 16.0 Hz), 7,36 (2H, d, J = 9.0 Hz), 7.31 (4H, m), 7.27 (1H, d, J = 16.5 Hz), 2.59 (3H, s), 2.33 (3H, s); MS (FAB) *m/z*: 504 ($[M+H]^+$); Anal. Calcd. for $C_{31}H_{25}N_3O_4 \cdot 3/2H_2O$: C, 70.18; H, 5.32; N, 7.92. Found: C, 70.46; H, 5.20; N, 8.10.

Angeli's salt (trioxodinitrate). Angeli's salt was prepared at >98% purity from butyl nitrate and hydroxylamine hydrochloride by the method of Smith and Hein:[1] $\varepsilon_{248\ \mathrm{nm}}$ obsd, 8200 M^{-1}cm^{-1} in 1 N NaOH; [lit.[2] 8300 M^{-1}cm^{-1}].

---

(1) Smith, P. A.; Hein, G. E. *J. Am. Chem. Soc.* **1960**, *82* (21), 5731–5740.

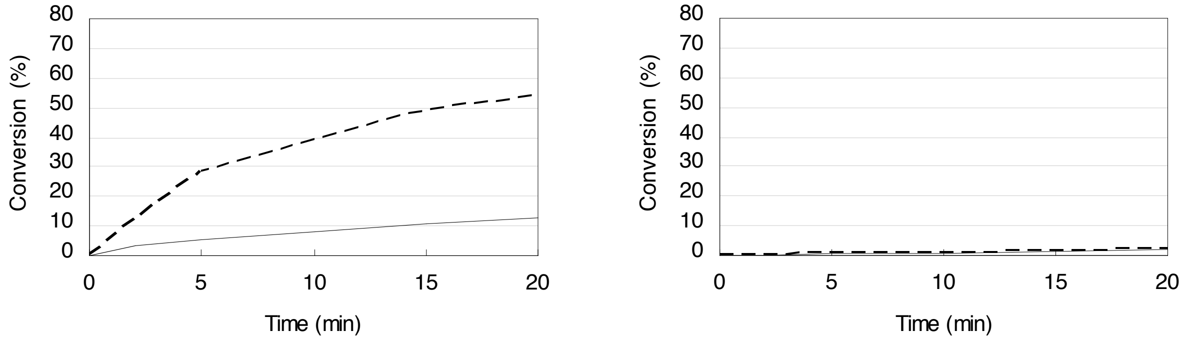
(2) Boghosian, R. A.; McGuinness, E. T. *Biochim. Biophys. Acta* **1979**, *567*, 278–286

<Analysis 1>

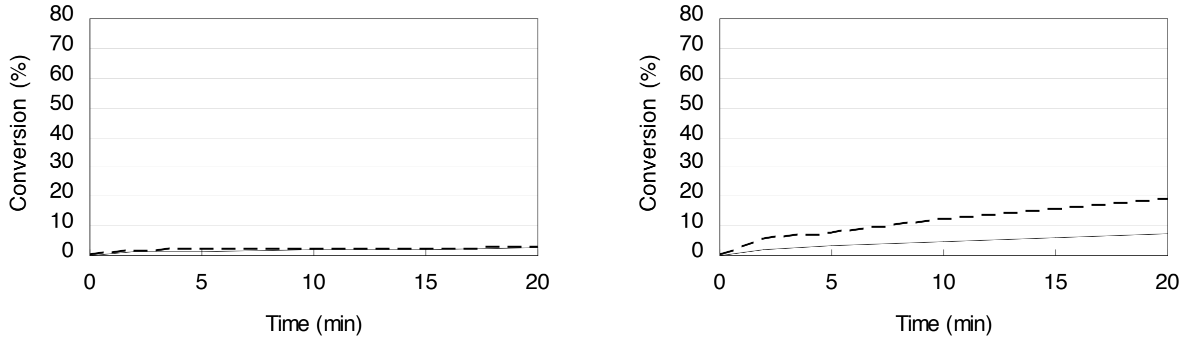
General Methods. Photoirradiation of ultraviolet A was performed by using the light-source (100 W mercury lamp) of a fluorescence microscope (Olympus BX60/BX-FLA) with a WU filter (330–380 nm band-pass filter) under Ar or He purged-anaerobic conditions . The light intensity was attenuated to 1.25% with a combination of 6% ND filter and 25% ND filter.

Measurement of Photoinduced Conversion by Absorption Spectral Change. A solution of a donor (1.5 mM, 20 μL) in acetonitrile was diluted with acetonitrile (1330 μL) and milli Q water (150 μL) and the solution was transferred into a cuvette. UV/vis spectra were recorded by using an Agilent 8453 spectrometer after 0, 2, 5, 10, 15, and 20 min of photoirradiation at room temperature.

Compound **1** Compound **2**



Compound **3** Compound **4**



Compound **5**

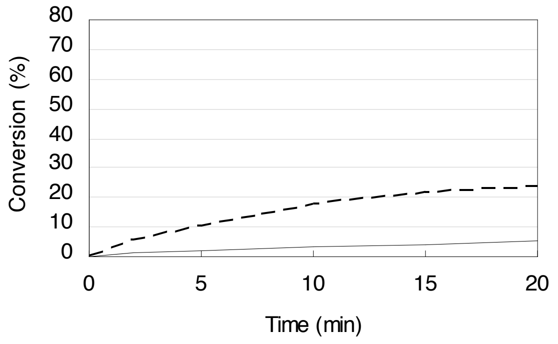


Figure S1. Conversion of cycloadducts (**1**–**5**) in acetonitrile/water (9:1) was calculated from the increase in the absorption of 9,10-DMA at 398 nm. The solid line shows conversion under dark conditions, and the dashed line shows conversion under photoirradiation.

Confirmation of retro-Diels-Alder Products by ^{1}H-NMR Measurement. A solution of donor (1.5 μmol) in DMSO-d_6 (900 μL) and D_2O (100 μL) was prepared. For the experiments to scavenge acyl nitroso derivatives, 2-mercaptoethanol (1.05 μL) was added to the solution. ^{1}H-NMR spectra of the solution were measured after photoirradiation at room temperature by using a JEOL JNM-LA500 spectrometer.

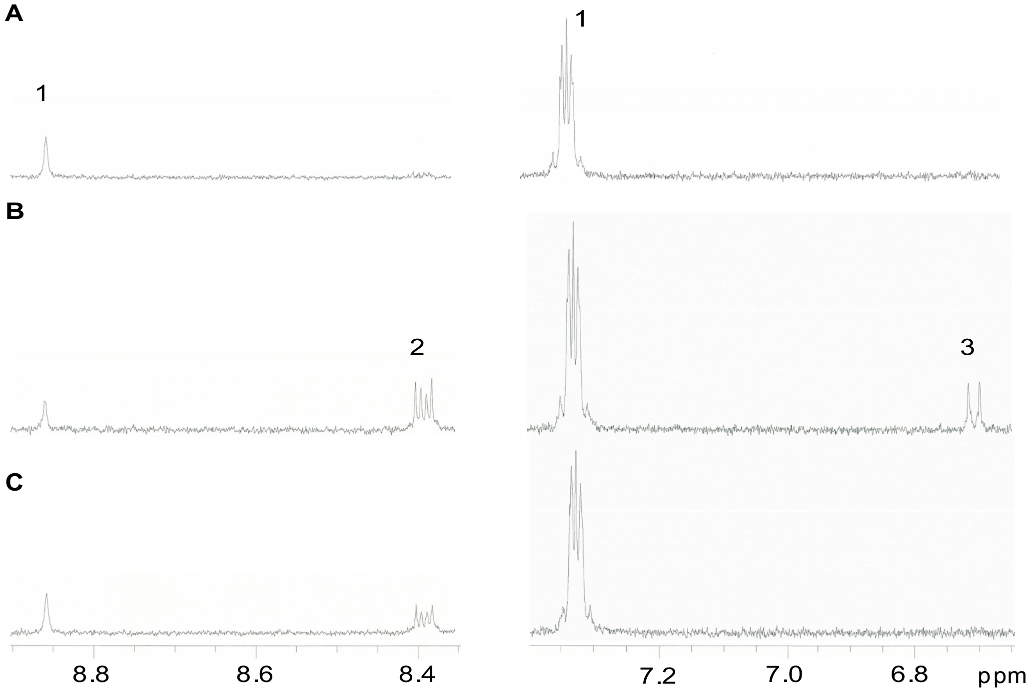


Figure S2. ^{1}H-NMR spectral change by photoinduced conversion of **5** in DMSO/water (9:1). Spectrum A was obtained just after preparing the solution, and spectrum B shows the same solution after 10 min of UV-A irradiation. Spectrum C shows the solution under the same conditions as those for B except for the addition of 2-ME. Each peak was labeled with a number such as 1, compound **5**; 2, 9,10-DMA; 3, the corresponding amine.