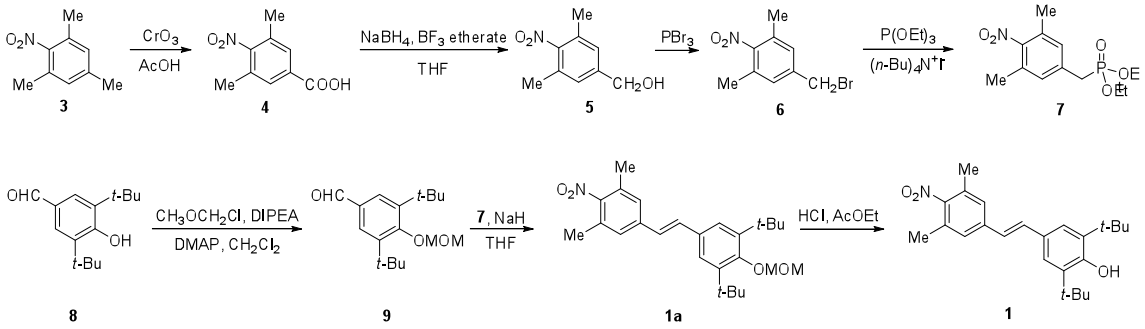
Supporting Information

General Method

Melting point was determined using a Büchi 545 melting point apparatus. Proton nuclear magnetic resonance spectra (^{1}H-NMR) and carbon nuclear magnetic resonance spectra (^{13}C-NMR) were recorded on a JEOL JNM-A500 spectrometer in the indicated solvent. Chemical shifts (δ) are reported in parts per million relative to the internal standard, tetramethylsilane. Elemental analysis was performed with Yanaco CHN CORDER NT-5 analyzer, and all values were within ±0.4 % of the calculated values. The MS spectra (EI-GC) were recorded on a JEOL JMS-SX102A mass spectrometer. Ultraviolet-visible-light absorbance spectra were recorded on an Agilent 8453 spectrometer. All other reagents and solvents were purchased from Aldrich, Tokyo Kasei Kogyo, Wako Pure Chemical Industries, Nacalai Tesque, Kanto Kagaku, Kishida Kagaku, and Dojindo, and used without purification. Flash column chromatography was performed using silica gel 60 (particle size 0.046-0.063 mm) supplied by Merck. Photoirradiation was performed using the light source of an Olympus BX-60 fluorescence microscope with a WU filter (330-380 nm band-pass filter). The light intensity was not attenuated. ESR spectra were taken on a JES-RE2X spectrometer (JEOL Co. Ltd., Tokyo, Japan). The fluorescence spectra were determined with a Hitachi F4500.

Experimental Section

Synthesis of **1**



Preparation of 3,5-dimethyl-4-nitrobenzoic acid (4)

To a slurry of CrO_3 (20.0 g, 200 mmol, 3.2 eq) in AcOH (220 mL) was added 2-nitromesitylene (**3**) (10.2 g, 61.8 mmol) dissolved in AcOH (30 mL). The mixture was stirred at room temperature for 12.5 hr. The mixture was poured into ice water to precipitate a white solid, which was collected by filtration and dissolved in $CHCl_3$. The $CHCl_3$ layer was washed with 2 N NaOH, and the aqueous layer was acidified with conc. HCl, and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with brine and dried over Na_2SO_4, and the solvent was removed by evaporation *in vacuo* to yield **4** (4.03

g, 34 %) as a colorless powder: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.90 (2H, s), 2.38 (6H, s).

Preparation of (3,5-dimethyl-4-nitrophenyl)methanol (5)

To a slurry of $NaBH_4$ (2.36 g, 62.3 mmol, 3.0 eq) in THF (40 mL) was added **4** (4.03 g, 20.7 mmol) dissolved in THF (30 mL) followed by BF_3 etherate (2.26 g, 15.9 mmol, 0.77 eq). The mixture was stirred at room temperature for 8 hr. The mixture was added to water and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 3.08 g (82 %) of **5** as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.12 (2H, s), 4.69 (2H, s), 2.32 (6H, s).

Preparation of 5-(bromomethyl)-1,3-dimethyl-2-nitrobenzene (6)

A mixture of PBr_3 (14.4 g, 53.2 mmol, 3.1 eq) and **5** (3.08 g, 17.0 mmol) was stirred at room temperature for 2 hr. The mixture was poured into water and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash column chromatography (*n*-hexane/AcOEt = 6:1) gave 3.29 g (81 %) of **6** as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.15 (2H, s), 4.41 (2H, s), 2.31 (6H, s).

Preparation of diethyl-(3,5-dimethyl-4-nitrobenzyl)phosphonate (7)

Tetrabutylammonium iodide (413 mg, 1.19 mmol, 0.080 eq) and triethylphosphite (2.98 g, 17.9 mmol, 1.3 eq) were added to **6** (3.29 g, 13.7 mmol). The mixture was stirred at 120 °C for 4.5 hr, then cooled to room temperature and purified by silica gel flash column chromatography (*n*-hexane/AcOEt = 1:9) to give 3.34 g (80 %) of **7** as a yellow oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.06 (2H, d, J = 2.3 Hz), 4.06 (4H, m), 3.09 (2H, d, J_{PH} = 21.9 Hz), 2.30 (6H, s), 1.28 (6H, t, J = 7.3 Hz).

Preparation of 3,5-di-*tert*-butyl-4-(methoxymethoxy)benzaldehyde (9)

To a solution of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (**8**) (6.03 g, 25.7 mmol) and DMAP (32 mg, 0.258 mmol, 0.01 eq) in CH_2Cl_2 (150 mL) was added DIPEA (5.66 g, 43.8 mmol, 1.7 eq), and then to this mixture was added MOMCl (2.46 g, 30.6 mmol, 1.2 eq). The whole was stirred at room temperature for 19 hr, then treated with 0.1 N HCl. The organic layer was separated and the aqueous solution was extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification by silica gel flash chromatography (*n*-hexane/AcOEt = 20:1) gave 1.55 g (22 %) of **9** as a colorless solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.92 (1H, s), 7.81 (2H, s), 4.94 (2H, s), 3.66 (3H, s), 1.48 (18H, s).

Preparation of 5-{(*E*)-2-[3,5-di-*tert*-butyl-4-(methoxymethoxy)phenyl]vinyl}-1,3-dimethyl-2-

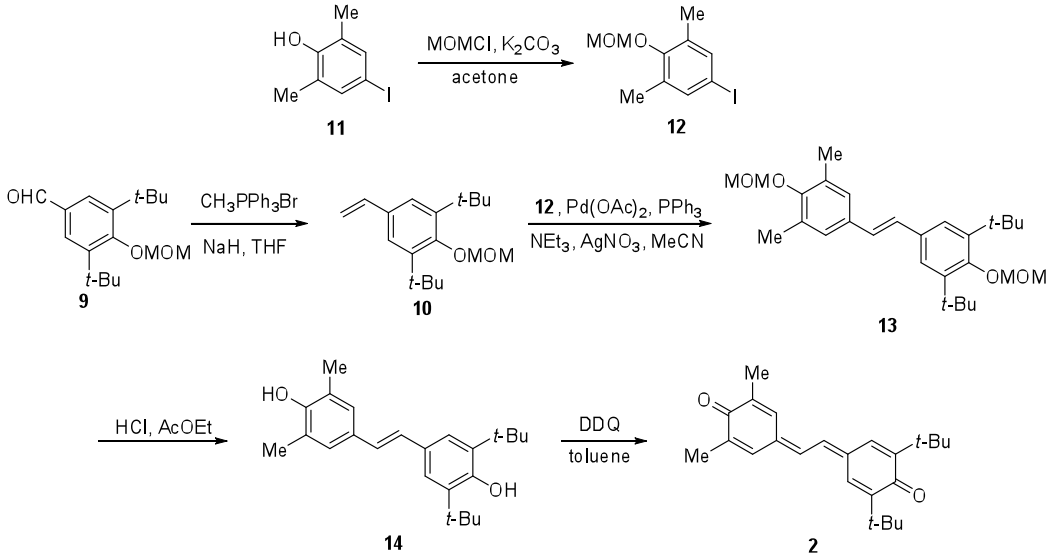
nitrobenzene (1a)

To a suspension of NaH (181 mg, 7.54 mmol, 2.7 eq) in THF (15 mL) was added **7** (1.01 g, 3.37 mmol, 1.2 eq) on an ice bath. The mixture was stirred at room temperature for 25 min. Then, to this mixture was added a solution of **9** (780 mg, 2.80 mmol) in THF (10 mL). The reaction mixture was stirred at room temperature for 5 hr, poured into water on an ice bath, and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* and purification by silica gel flash chromatography (*n*-hexane/AcOEt = 20:1) gave 1.06 g (89 %) of **1a** as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.42 (2H, s), 7.25 (2H, s), 7.10 (1H, d, J = 16.4 Hz), 6.90 (1H, d, J = 16.1 Hz), 4.92 (2H, s), 3.66 (3H, s), 2.35 (6H, s), 1.48 (18H, s).

Preparation of 4-[(*E*)-2-(3,5-dimethyl-4-nitrophenyl)vinyl]-3,5-di-*tert*-butylphenol (1)

To a solution of **1a** (1.06 g, 2.50 mmol) in AcOEt (5 mL) was added 4 N HCl-AcOEt (10 mL). The mixture was stirred at room temperature for 2.5 hr. The mixture was poured into sat. $NaHCO_3$ and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 944 mg (99 %) of **1** as a yellow amorphous solid, which was recrystallized from *n*-hexane to yield 676 mg (72 %) of **1** as yellow crystals: mp 168.7-169.5 °C; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.35 (2H, s), 7.23 (2H, s), 7.10 (1H, d, J = 16.4 Hz), 6.85 (1H, d, J = 16.1 Hz), 5.35 (1H, s), 2.34 (6H, s), 1.48 (18H, s); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 154.4, 150.2, 139.8, 136.3, 132.1, 130.3, 127.9, 126.4, 123.8, 123.7, 34.4, 30.3, 17.9; Anal.Calcd for $C_{24}H_{31}NO_3$; C:75.56, H:8.19, N:3.67. Found ; C:75.38, H:8.24, N:3.59; MS (EI-GC) : m/z 381 (M^+).

Synthesis of **2**



Preparation of 4-(methoxymethoxy)-2,6-dimethyliodobenzene (12)

To a solution of 2,6-dimethyl-4-iodophenol (**11**) (1.66 g, 6.70 mmol) in acetone (15 mL) was added K_2CO_3 (1.87 g, 13.5 mmol, 2.0 eq). This mixture was stirred at room temperature for 15 min. To this solution, MOMCl (1.08 g, 12.7 mmol, 1.9 eq) was added slowly. After complete addition, the mixture was warmed to reflux for 5.5 hr. Again, the reaction mixture was cooled to room temperature. After removal of excess K_2CO_3 by filtration on a Kiriyama funnel, the solution was poured into water and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 20:1) gave 771 mg (39 %) of **12** as a colorless oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.35 (2H, s), 4.93 (2H, s), 3.59 (3H, s), 2.24 (6H, s).

Preparation of 3,5-di-*tert*-butyl-4-(methoxymethoxy)ethenylbenzene (10)

To a suspension of CH_3PPh_3Br (1.79 g, 5.01 mmol, 1.0 eq) in dry THF (10 mL) was added a suspension of NaH (60% in oil; 262 mg, 6.55 mmol, 1.3 eq) in dry THF (10 mL) and **9** (1.39 g, 5.00 mmol) in dry THF (10 mL). The reaction mixture was stirred at room temperature for 2 hr, then poured into water and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 40:1) gave 506 mg (37 %) of **10** as a yellow oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.31 (2H, s), 6.67 (1H, dd, J = 11.0 Hz, 17.7 Hz), 5.63 (1H, dd, J = 0.6 Hz, 17.7 Hz), 5.17 (1H, dd, J = 0.8 Hz, 10.8 Hz), 4.89 (2H, s), 3.64 (3H, s), 1.45 (18H, s).

Preparation of 4-{(*E*)-2-[3,5-di-*tert*-butyl-4-(methoxymethoxy)phenyl]ethenyl}-2,6-dimethyl-4-(methoxymethoxy)benzene (13)

To acetonitrile (15 mL) were added **12** (506 mg, 1.83 mmol), **10** (590 mg, 2.02 mmol, 1.1 eq), $Pd(OAc)_2$ (44 mg, 0.196 mmol, 0.1 eq), PPh_3 (103 mg, 0.393 mmol, 0.2 eq), NEt_3 (185 mg, 1.83 mmol, 1.0 eq), and $AgNO_3$ (355 mg, 2.09 mmol, 1.1 eq). The mixture was stirred at room temperature for 1.5 hr, heated at 100 °C for 3 hr, then filtered. The filtrate was poured into water and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/toluene = 6:1) gave 636 mg (79 %) of **13** as a brown oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.39 (2H, s), 7.18 (2H, s), 6.97 (1H, d, J = 16.1 Hz), 6.88 (1H, d, J = 16.1 Hz), 4.97 (2H, s), 4.91 (2H, s), 3.65 (3H, s), 3.62 (3H, s), 2.31 (6H, s), 1.47 (18H, s).

Preparation of 4-[(*E*)-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethenyl]-3,5-dimethylphenol (14)

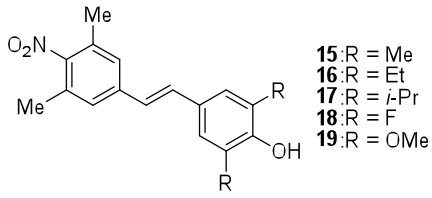
To a solution of **13** (636 mg, 1.44 mmol) in AcOEt (5 mL) was added 4 N HCl-AcOEt (5 mL). The mixture was stirred at room temperature for 1 hr, then poured into water and extracted. The organic

layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 6:1) gave 295 mg (58 %) of **14** as a brown solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.31 (2H, s), 7.15 (2H, s), 6.92 (1H, d, *J* = 16.1 Hz), 6.83 (1H, d, *J* = 16.1 Hz), 5.23 (1H, s), 4.60 (1H, s), 2.27 (6H, s), 1.47 (18H, s).

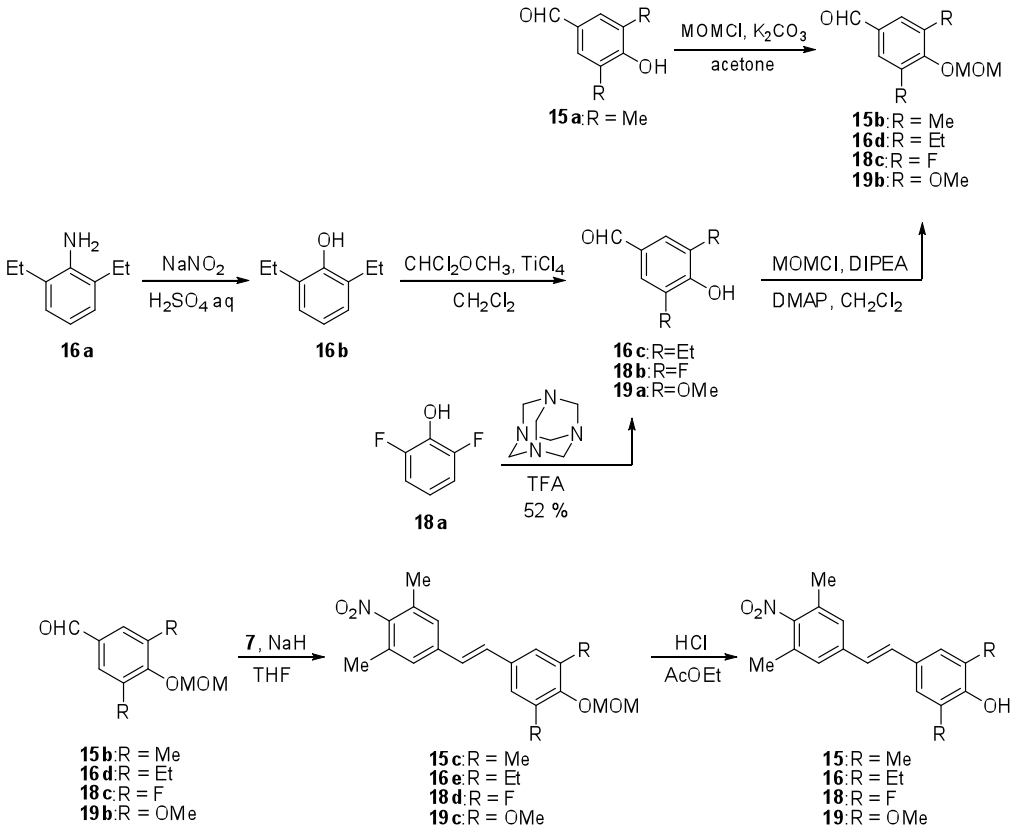
Preparation of 4-[2-(3,5-di-*tert*-butyl-4-oxocyclohexa-2,5-dien-1-ylidene)ethylidene]-2,6-dimethylcyclohexa-2,5-dien-1-one (2)

To a solution of **14** (295 mg, 0.837 mmol) in toluene (10 mL) was added DDQ (199 mg, 0.877 mmol, 1.0 eq). The mixture was stirred at room temperature for 1.5 hr. The solvent was removed by evaporation *in vacuo*. The residue was purified by silica gel flash chromatography (*n*-hexane/AcOEt = 6:1) to afford 229 mg (78 %) of **2** as a red solid, which was recrystallized from *n*-hexane/AcOEt and gave 168 mg (73 %) of **2** as a violet solid: mp 196.0-197.0 ºC; ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 7.98 (1H, s), 7.89 (1H, d, *J* = 13.4 Hz), 7.80 (1H, d, *J* = 13.4 Hz), 7.70 (1H, s), 7.43 (1H, s), 7.29 (1H, s), 2.02 (3H, s), 1.98 (3H, s), 1.31 (9H, s), 1.28 (9H, s); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm), 182.2, 158.3, 150.3, 150.0, 138.2, 137.7, 137.6, 136.7, 134.1, 133.3, 133.3, 128.2, 124.4, 99.0, 94.7, 84.8, 63.0, 35.8, 35.4, 29.6, 29.6, 17.0, 16.4; Anal.Calcd for $C_{24}H_{30}O_2$; C:82.24, H:8.53. Found ; C:82.04, H:8.53; MS (EI-GC) m/z 350 (M^+).

Synthesis of **15**-**19**



15:R = Me
16:R = Et
17:R = *i*-Pr
18:R = F
19:R = OMe



Preparation of 4-(methoxymethoxy)-3,5-dimethylbenzaldehyde (15b).

To a solution of 3,5-dimethyl-4-hydroxybenzaldehyde (**15a**) (1.36 g, 9.02 mmol) in acetone 17 mL was added K_2CO_3 (2.53 g, 2.0 eq). This solution was stirred at room temperature for 15 min. To this solution, MOMCl (725 mg, 9.00 mmol, 1.0 eq) was added slowly by syringe through a septum. After complete addition, the reaction mixture was warmed to reflux temperature for 2 hr, then cooled to room temperature. After removal of excess K_2CO_3 by filtration on a Kiriyama funnel, the filtrate was evaporated under reduced pressure to give 1.75 g (q. y.) of **15b** as a yellow oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.89 (1H,s), 7.57 (2H, s), 5.03 (2H, s), 3.62 (3H, s), 2.36 (6H, s).

Preparation of 5-[(*E*)-2-(3,5-dimethyl-4-nitrophenyl)vinyl]-2-(methoxymethoxy)-1,3-dimethyl-benzene (15c).

To a solution of NaH (60% in oil; 35 mg, 13.96 mg, 1.7 eq) in THF (5 mL) was added **7** (2.47 g, 8.20 mmol) in THF (5 mL). The mixture was stirred at room temperature for 3 hr, then a solution of **15b** (1.70 g, 8.75 mmol, 1.1 eq) in THF (5 mL) was added. The reaction mixture was stirred at room temperature for 24 h, then poured into water and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash column chromatography (*n*-hexane/AcOEt = 20:1) gave 2.11 g (75 %) of

15c as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.22 (2H, s), 7.19 (2H, s) 7.03 (1H, d, *J* = 16.1 Hz), 6.91 (1H, d, *J* = 16.4 Hz), 4.98 (2H, s), 3.62 (3H, s), 2.34 (6H, s), 2.32 (6H, s).

Preparation of 4-[(*E*)-2-(3,5-dimethyl-4-nitrophenyl)vinyl]-2,6-dimethylphenol (15).

To a solution of **15c** (2.04 g, 5.96 mmol) in AcOEt and $CHCl_3$ (15 mL and 5 mL) was added 4 N HCl-AcOEt (20 mL). The mixture was stirred at room temperature for 1 hr, then poured into water and extracted with AcOEt. The AcOEt layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 1.72 g (97 %) of **15** as a yellow solid, which was recrystallized from AcOEt to give 464 mg (27 %) of **15** as yellow crystals: mp 230.2-234.2 °C; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.20, (2H, s), 7.16 (2H, s), 7.02 (1H, d, *J* = 16.1 Hz), 6.86 (1H, d, *J* = 16.1 Hz), 4.71 (1H), 2.34 (6H, s), 2.28 (6H, s); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 152.7, 150.3, 139.7, 131.1, 130.3, 128.9, 127.3, 126.4, 124.1, 123.4, 17.9, 16.0; Anal.Calcd for $C_{18}H_{19}NO_3$; C:72.71, H:6.44, N:4.71. Found ; C:72.71, H:6.55, N:4.78; MS (EI-GC) m/z 297 (M^+).

Preparation of 2,6-diethylphenol (16b)

2,6-Diethylaniline (**16a**) (3.00 g, 20.0 mmol) was dissolved in water (60 mL) and conc. H_2SO_4 (40 mL) in a 1 L flask with a stirring bar on an ice bath. $NaNO_2$ (1.54 g, 22.3 mmol, 1.1 eq) was dissolved in water (40 mL), and the solution was added slowly to the reaction mixture. The solution turned light orange, and bubbles of N_2 were observed. The solution was added to 50 % sulfuric acid (50 mL), and the mixture was heated to 90-100 °C for 15 min, then extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/toluene = 4/1 → 3/1) gave 2.18 g (72 %) of **16b** as a clear solid; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.00 (2H, d, *J* = 7.6 Hz), 6.84 (1H, t, *J* = 7.6 Hz), 4.65 (1H, s), 2.63 (4H, q, *J* = 7.6 Hz), 1.25 (6H, t, *J* = 7.6 Hz).

Preparation of 3,5-diethyl-4-hydroxybenzaldehyde (16c)

To a solution of **16b** (2.18 g, 14.5 mmol) was added $TiCl_4$ (6.06 g, 31.9 mmol, 2.2 eq) followed by $CHCl_2OCH_3$ (1.84 g, 16.0 mmol, 1.1 eq) on an ice bath. The reaction mixture was stirred at room temperature for 3 hr, then poured into water on an ice bath and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 6/1) gave 1.78 g (69 %) of **16c** as a yellow solid; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.85 (1H, s), 7.57 (2H, s), 5.29 (1H, s), 2.69 (4H, q, *J* = 7.6 Hz), 1.29 (6H, t, *J* = 7.6 Hz).

Preparation of 3,5-diethyl-4-(methoxymethoxy)benzaldehyde (16d)

To a mixture of **16c** (254 mg, 1.425 mmol), DMAP (5 mg, 0.0041 mmol, 0.03 eq), DIPEA (304 mg,

2.35 mmol, 1.7 eq) in CH_2Cl_2 (10 mL) maintained at 0 °C (ice-water bath) was added MOMCl (137 mg, 1.71 mmol, 1.2 eq). After complete addition, the reaction mixture was allowed to warm to room temperature and then stirred for 2 hr, followed by treatment with 0.1 N HCl. The organic layer was separated, washed with brine, and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 4/1) gave 253 mg (80 %) of **16d** as a yellow oil; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.93 (1H, s), 7.62 (2H, s), 5.00 (2H, s), 3.63 (3H, s), 2.75 (4H, q, *J* = 7.6 Hz), 1.27 (6H, t, *J* = 7.6 Hz).

Preparation of 4-{(E)-[3,5-diethyl-4-(methoxymethoxy)]vinyl}-2,6-dimethylnitrobenzene (16e)

To a solution of **7** (517 mg, 1.72 mmol, 1.5 eq) in THF (8 mL) was added NaH (66 mg, 2.75 mmol, 2.4 eq). The mixture was stirred at room temperature for 15 min, then **16d** (253 mg, 1.14 mmol) in THF (5 mL) was added and stirring was continued at room temperature for 2.5 hr. The reaction mixture was poured into water and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 6/1) gave 401 mg (95 %) of **16e** as a yellow solid; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.24 (2H, s), 7.23 (2H, s), 7.09 (1H, d, *J* = 16.4 Hz), 6.93 (1H, d, *J* = 16.1 Hz), 4.97 (2H, s), 3.62 (3H, s), 2.71 (4H, q, *J* = 7.6 Hz), 2.35 (6H, s), 1.27 (6H, t, *J* = 7.6 Hz).

Preparation of 4-[(E)-(3,5-dimethyl-4-nitrophenyl)vinyl]-2,6-diethylphenol (16)

To a solution of **16e** (401 mg, 1.09 mmol) in AcOEt added 4 N HCl-AcOEt (5 mL). The mixture was stirred at room temperature for 1 hr, then poured into water and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 338 mg (96 %) of **16** as a yellow solid, which was recrystallized from *n*-hexane/toluene/ AcOEt 221 mg (65 %) to afford a yellow solid: mp 158.5-162.8 °C; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.22 (2H, s), 7.18 (2H, s), 7.07 (1H, d, *J* = 16.4 Hz), 6.88 (1H, d, *J* = 16.1 Hz), 4.84 (1H, s), 2.66 (4H, q, *J* = 7.6 Hz), 2.34 (6H, s), 1.29 (6H, t, *J* = 7.6 Hz); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 151.8, 150.3, 139.7, 131.4, 130.3, 129.6, 129.1, 126.4, 125.4, 124.1, 23.1, 17.9, 13.9; Anal. Calcd. for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.79; H, 7.24; N, 4.40.

Preparation of 3,5-difluoro-4-hydroxybenzaldehyde (18b)

A stirred solution of 2,6-difluorophenol (**18a**) (2.11 g, 16.2 mmol) and hexamethylenetetramine (2.35 g, 16.7 mmol, 1.0 eq) in TFA (30 mL) was heated at reflux under Ar for 24 hr, then cooled to room temperature. The solvent was evaporated *in vacuo* and the crude residue was suspended in $CHCl_3$. The suspension was washed with an aqueous solution of sat. $NaHCO_3$ and the separated aqueous layer was acidified with conc. HCl. The aqueous layer was extracted with $CHCl_3$. The

organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to afford 1.33 g (52 %) of **18b** as a colorless solid. ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.82 (1H, t, J_{FH} = 1.8 Hz), 7.49 (2H, d, J_{FH} = 6.4 Hz).

Preparation of 3,5-difluoro-4-(methoxymethoxy)benzaldehyde (18c).

A stirred mixture of **18b** (300 mg, 1.90 mmol), DMAP (8 mg, 0.0655 mmol, 0.03 eq), and DIPEA (392 mg, 3.04 mmol, 1.6 eq) in CH_2Cl_2 (15 mL) maintained at 0 °C (ice-water bath) under an atmosphere of Ar was treated dropwise with MOMCl (183 mg, 2.28 mmol, 1.2 eq). After complete addition, the reaction mixture was allowed to warm to room temperature and then stirred for 1.5 hr. The reaction mixture was added to $CHCl_3$ and washed with 0.1 N HCl. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 351 mg (92 %) of **18c** as a yellow oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.86 (1H, t, J_{FH} = 1.8 Hz), 7.47 (2H, d, J_{FH} = 8.2 Hz), 5.29 (2H, s), 3.60 (3H, s).

Preparation of 4-{(*E*)-[3,5-difluoro-4-(methoxymethoxy)]vinyl}-2,6-dimethylnitrobenzene (18d).

To a solution of **7** (471 mg, 1.56 mmol) in THF (3 mL) was added NaH (60% in oil; 57 mg, 2.36 mmol, 1.6 eq). The mixture was stirred at room temperature for 10 min, then **18c** (303 mg, 1.50 mmol) in THF (2 mL) was added, and stirring was continued at room temperature for 2 hr. The mixture was poured into water and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 4:1) gave 476 mg (91 %) of **18d** as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.23 (2H, s), 7.06 (2H, d, J_{FH} = 8.8 Hz), 6.97 (1H, d, J = 16.1 Hz), 6.91 (1H, d, J = 16.1 Hz), 5.18 (2H, s), 3.61 (3H, s), 2.35 (6H, s).

Preparation of 4-[(*E*)-(3,5-dimethyl-4-nitrophenyl)vinyl]-2,6-difluorophenol (18).

To a solution of **18d** (476 mg, 1.36 mmol) in AcOEt (5 mL) was added TFA (5 mL). The reaction mixture was poured into water and extracted with AcOEt, The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 497 mg (q.y.) of **18** as a yellow solid, which was recrystallized from *n*-hexane/AcOEt to yield 173 mg (35 %) of **18** as yellow crystals: mp 214.7-218.3 °C; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.21 (2H, s), 7.07 (2H, d, J_{FH} = 8.8 Hz), 6.95 (1H, d, J = 16.3 Hz), 6.87 (1H, d, J = 16.4 Hz), 5.81 (1H, s), 2.35 (6H, s); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 152.8, 150.9, 132.7, 130.4, 129.1, 128.9, 127.2, 126.8, 109.9, 109.7, 17.7; Anal.Calcd for $C_{16}H_{13}F_2NO_3 \cdot 1/2H_2O$; C:61.15, H:4.49, N:4.46. Found ; C:61.12, H:4.43, N:4.30; MS (EI-GC) m/z 305 (M^+).

Preparation of 3,5-dimethoxy-4-(methoxymethoxy)benzaldehyde (19b).

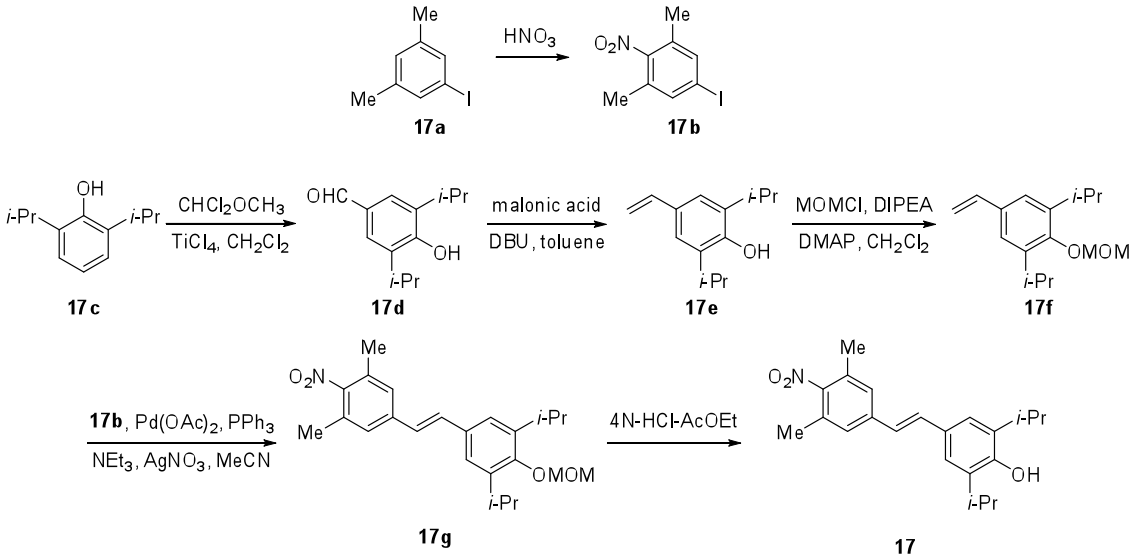
A stirred mixture of 3,5-dimethoxy-4-hydroxybenzaldehyde (**19a**) (512 mg, 2.81 mmol), DMAP (4 mg, 0.0327 mmol, 0.01 eq), and DIPEA (586 mg, 4.53 mmol, 1.6 eq) in CH_2Cl_2 (10 mL) maintained at 0 °C (ice-water bath) under an atmosphere of argon was treated dropwise with MOMCl (271 mg, 3.37 mmol, 1.2 eq). After complete addition, the reaction mixture was allowed to warm to room temperature and then stirred for 1.5 hr, followed by addition of HCl (15 mL of 0.1 M aqueous solution). The CH_2Cl_2 layer was separated, and the aqueous layer was extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 3:2) gave 497 mg (78 %) of **19b** as a colorless solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.88 (1H, s), 7.14 (2H, s), 5.23 (2H, s), 3.93 (6H, s), 3.60 (3H, s).

Preparation of 5-{(*E*)-2-[3,5-dimethoxy-4-(methoxymethoxy)phenyl]vinyl}-1,3-dimethyl-2-nitrobenzene (19c).

To a solution of **7** (629 mg, 2.09 mmol) in THF (5 mL) was added NaH (60% in oil; 70 mg, 2.93 mmol, 1.4 eq). The mixture was stirred at room temperature for 15 min, then a solution of **19b** (495 mg, 2.19 mmol) in THF (5 mL) was added, and stirring was continued at room temperature for 5 hr. The mixture was poured into water and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 5:1) gave 342 mg (65 %) of **19c** as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.25 (2H, s), 7.07 (1H, d, J = 16.4 Hz), 6.92 (1H, d, J = 16.1 Hz), 6.75 (2H, s), 5.15 (2H, s), 3.91 (6H, s), 2.35 (6H, s).

Preparation of 4-[(*E*)-2-(3,5-dimethyl-4-nitrophenyl)vinyl]-3,5-dimethoxyphenol (19).

To a solution of **19c** (520 mg, 1.39 mmol) in AcOEt (15 mL) was added 4 N HCl-AcOEt (5 mL). The mixture was stirred at room temperature for 2 hr, then poured into water and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 456 mg (99 %) of **19** as a yellow solid, which was recrystallized from *n*-hexane/AcOEt to yield 359 mg (79 %) of **19** as a yellow solid: mp 217.2-219.2 °C; ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.23 (2H, s), 7.06 (1H, d, J = 16.4 Hz), 6.88 (1H, d, J = 16.4 Hz), 6.76 (2H, s), 5.61 (1H, s), 3.95 (6H, s), 2.35 (6H, s); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 150.5, 147.3, 139.3, 135.5, 131.4, 130.3, 128.2, 126.5, 124.8, 103.7, 56.4, 16.8; Anal.Calcd for $C_{18}H_{19}NO_5$; C:65.54, H:5.81, N:4.25. Found ; C:65.46, H:5.90, N:4.26; MS (EI-GC) : m/z 329 (M^+).



Preparation of 3,5-dimethyl-4-nitroiodobenzene (17b).

To conc. HNO_3 aq. (7 mL) was added 3,5-dimethyliodobenzene (**17a**) (2.00 g, 8.62 mmol) at 0 °C. The mixture was heated to 50 °C for 9 hr and 80 °C for 12 hr, then poured onto ice, neutralized with sat. $NaHCO_3$ and extracted with Et_2O. The Et_2O layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (*n*-hexane/toluene = 20:1) gave 542 mg (23 %) of **17b** as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.51 (2H, s), 2.27 (6H, s).

Preparation of 3,5-diisopropyl-4-hydroxybenzaldehyde (17d)

To a solution of 2,6-diisopropylphenol (**17c**) (150 mg, 0.840 mmol) in CH_2Cl_2 was added $TiCl_4$ (351 mg, 1.85 mmol, 2.2 eq) followed by $CHCl_2OCH_3$ (106 mg, 0.924 mmol, 1.1 eq). The reaction mixture was stirred at room temperature for 3 hr, then poured into water and extracted with $CHCl_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* and purification of the residue by silica gel flash chromatography (n-hexane : AcOEt = 1:6) gave 112 mg (75 %) of **17d** as a yellow solid. ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 9.87 (1H, s), 7.63 (2H, s), 5.39 (1H, s), 3.17 (2H, sept, J = 7.0 Hz) 1.31 (12H, d, J = 7.0 Hz).

Preparation of 2,6-diisopropyl-4-vinylbenzaldehyde (17e).

To a solution of 3,5-diisopropyl-4-hydroxybenzaldehyde (**17d**) (403 mg, 1.96 mmol) and malonic acid (1.19 g, 11.4 mmol, 5.8 eq) in toluene (10 mL) was added DBU (298 mg, 1.96 mmol, 1.0 eq). The stirred reaction mixture was heated at reflux temperature (120 °C) for 16 hr, then cooled to room temperature. The reaction mixture was added to AcOEt, and washed with an aqueous solution

of sat.$NaHCO_3$. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation and purification of the residue by silica gel flash chromatography (*n*-hexane/AcOEt = 20:1) gave 296 mg (74 %) of **17e** as a colorless oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.12 (2H, s), 6.69-6.63 (1H, dd, *J* = 11.0 Hz, 17.7 Hz), 5.61 (1H, d, *J* = 17.4 Hz), 5.11 (1H, d, *J* = 11.0 Hz), 4.81 (1H, s), 3.14 (2H, sept, *J* = 6.7 Hz), 1.28 (12H, d, *J* = 7.0 Hz).

Preparation of 3,5-diisopropyl-4-(methoxymethoxy)vinylbenzene (17f).

A magnetically stirred mixture of **17e** (296 mg, 1.45 mmol), DMAP (4 mg, 0.0327 mmol, 0.02 eq), and DIPEA (300 mg, 2.32 mmol, 1.6 eq) in CH_2Cl_2 (5 mL) maintained at 0 °C (ice-water bath) under an atmosphere of Ar was treated dropwise with MOMCl (280 mg, 3.48 mmol, 2.4 eq). After complete addition, the reaction mixture was allowed to warm to room temperature and then stirred for 4 hr. The reaction mixture was added to $CHCl_3$ and extracted with 0.1 N HCl. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 165 mg (46 %) of **17f** as a colorless oil: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 7.15 (2H, s), 6.71-6.66 (1H, dd, J = 11.0 Hz, 17.7 Hz), 5.67 (1H, d, J = 17.7 Hz), 5.19 (1H, d, 10.1 Hz), 4.92 (2H, s), 3.62 (3H, s), 3.37-3.29 (2H, sept, *J* = 7.0 Hz), 1.24 (12H, d, *J* = 7.0 Hz).

Preparation of 4-{(*E*)-[3,5-diisopropyl-4-(methoxymethoxy)]vinyl}-2,6-dimethylnitrobenzene (17g).

To a solution of **17f** (162 mg, 0.650 mmol) in CH_3CN (6 mL) was added a solution of **17b** (200 mg, 0.721 mmol, 1.1 eq) in CH_3CN (4 mL), $Pd(OAc)_2$ (15 mg, 0.0668 mmol, 0.1 eq), PPh_3 (34 mg, 0.131 mmol, 0.2 eq), NEt_3 (66 mg, 0.651 mmol, 1.0 eq), and $AgNO_3$ (122 mg, 0.715 mmol, 1.1 eq). The mixture was stirred at room temperature for 1.5 hr, heated at 100 °C for 3 hr, then filtered and poured into water. After extraction with $CHCl_3$, the organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation, and purification of the residue by silica gel flash chromatography (*n*-hexane/toluene = 1:1) gave 202 mg (78 %) of **17g** as a yellow amorphous solid: ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 7.54 (2H, s), 7.40 (2H, s), 7.37 (1H, d, *J* = 16.8 Hz), 7.21 (1H, d, *J* = 16.4 Hz), 4.91 (2H, s), 3.52 (3H, s), 3.29 (2H, sept, *J* = 7.3 Hz), 2.29 (6H, s), 1.21 (12H, d, *J* = 7.0 Hz).

Preparation of 4-[(*E*)-(3,5-dimethyl-4-nitrophenyl)vinyl]-2,6-diisopropylphenol (17).

To a solution of **17g** (189 mg, 0.476 mmol) in AcOEt (3 mL) was added 4 N HCl-AcOEt (3 mL). The mixture was stirred at room temperature for 1.5 hr, then poured into water and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* gave 162 mg (97 %) of **17** as a yellow solid, which was recrystallized from *n*-hexane/toluene to yield 113 mg (70 %) of **17** as yellow crystals: mp 160.2-163.0 ºC; ^{1}H-NMR

($CDCl_3$, 500 MHz, δ; ppm) 7.24 (2H, s), 7.23 (2H, s), 7.11 (1H, d, J = 16.1 Hz), 6.88 (1H, d, J = 16.1 Hz), 4.91 (1H, s), 3.17 (2H, sept, J = 7.0 Hz), 2.35 (6H, s), 1.31 (12H, d, J = 6.7 Hz); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 150.6, 150.3, 139.8, 134.1, 131.8, 130.3, 129.1, 126.4, 123.9, 122.3, 27.3, 22.7, 17.9; Anal. Calcd. for $C_{20}H_{23}NO_3$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.44; H, 7.70; N, 4.05; MS (EI-GC) m/z 353 (M^+).

Fluorescence measurement by using HKGreen-3

Samples containing 10 μM **1** and 10 μM HKGreen-3 in potassium phosphate buffer (100 mM, pH 7.4, containing 1.1 % DMF) were irradiated for 15 min under aerobic or anaerobic conditions. The fluorescence intensity was determined at 515 nm with excitation at 490 nm. The slit width was set to 2.5 nm for both excitation and emission. The photomultiplier voltage was 950 V.

Assay for DNA strand breaks

Samples were solutions (total volume 20 μL) of 10 mM potassium phosphate buffer, containing 0.04 mg/mL of pBR 322 DNA, DMF 1% and 100 μM **1** or 300 μM $ONOO^-$ solution. After photoirradiation or incubation, the reaction mixtures were treated with 5 μL of loading buffer. Horizontal gel electrophoresis was carried out in 89 mM TBE buffer, pH 8.3, for 30 min at 50 V then for 30 min at 100 V. The gel was stained with ethidium bromide (1 mg/mL) for 30 min, destained in TBE buffer for 30 min, and photographed with UV translumination.

NO_2^-/NO_3^- concentration measurement

A solution of **1** (10 μM) in buffer solution of NO_2^-/NO_3^- Assay-kit FX (containing 0.1 % DMF) was photoirradiated for 15 min. Formed **2** and remaining **1** were removed on an OASIS column (Waters), and the pass-through fraction was analyzed with a NO_2^-/NO_3^- Assay-kit FX (Dojindo).

Figures and Tables

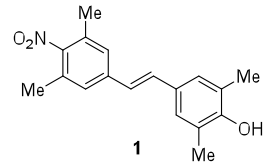
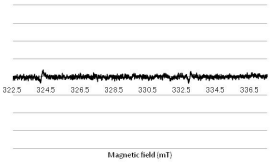
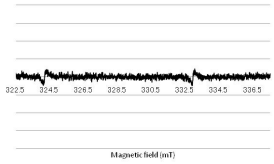
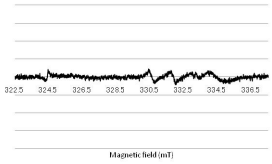
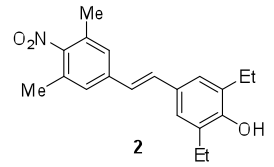
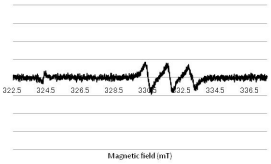
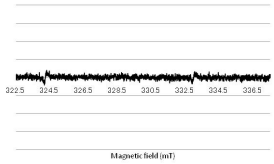
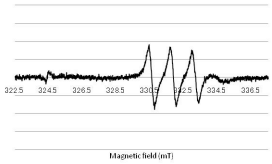
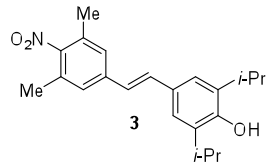
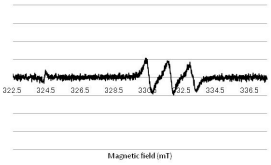
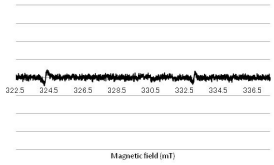
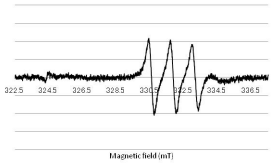
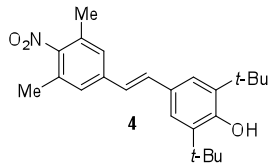
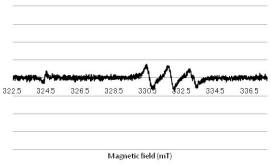
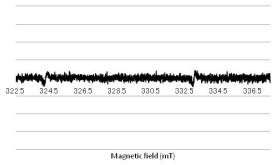
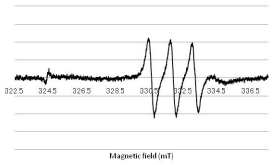
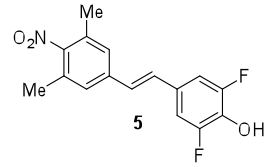
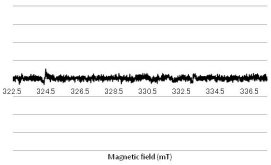
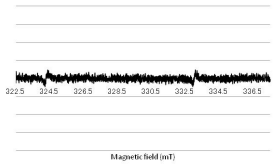
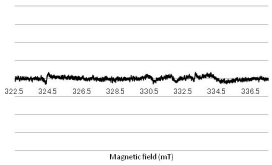
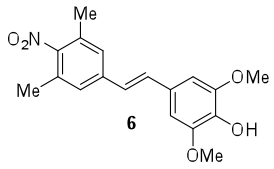
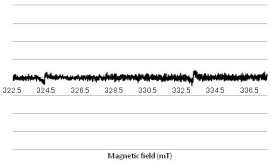
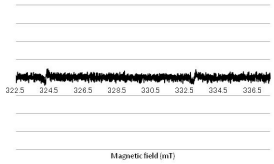
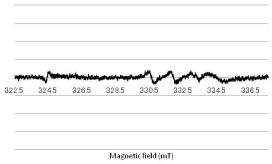
Compound	(a) Anaerobic	(b) Aerobic	(c) Addition of SOD
 **1**			
 **2**			
 **3**			
 **4**			
 **5**			
 **6**			

Figure S1. ESR spectra of [$(MGD)_2$-Fe-NO] complex of sample solutions after photo-irradiation: (a) Sample solutions containing 100 μM **1**, **15-19**, 1.5 mM $FeSO_4$, and 6 mM MGD in PBS (10 mM, pH 7.5) containing 1% DMF were photo-irradiated under an Ar atmosphere (anaerobic); (b) Sample solutions were the same as in (a), but were photo-irradiated under aerobic conditions; (c) Sample solutions containing 100 μM **1**, **15-19**, 1.5 mM $FeSO_4$, MGD 6 mM, and 1 kU/mL SOD in PBS (10 mM, pH 7.5) with 1% DMF were photo-irradiated under aerobic conditions for 15 min: The ESR measurement conditions were as follows; microwave power, 10 mW; frequency, 9.4200 GHz; field, 330 mT; sweep width, 7.5 mT; sweep time, 4 min; modulation width, 0.125 mT; time constant; 0.10 s.

Table S1. Photo-decomposition of synthesized compounds determined by HPLC

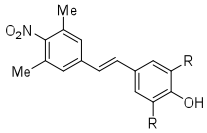
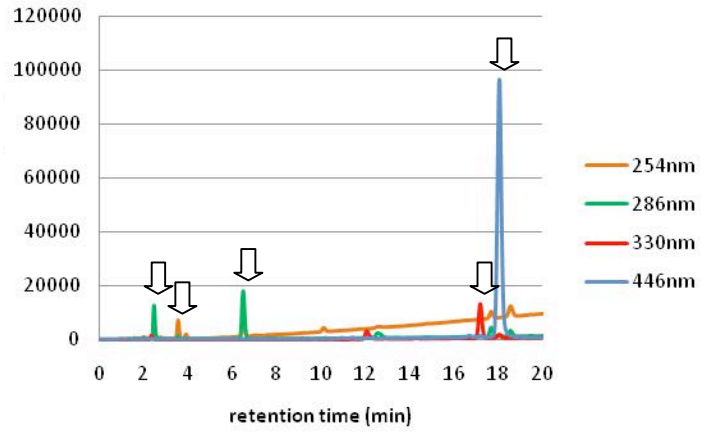
Compound	**15**	**16**	**17**	**1**	**18**	**19**
Substituent (R) 	Me	Et	*i*-Pr	*t*-Bu	F	OMe
Photo-decomposition ratio **(%)**	20.3 %	39.6 %	97.5 %	98.0 %	42.4 %	14.3 %

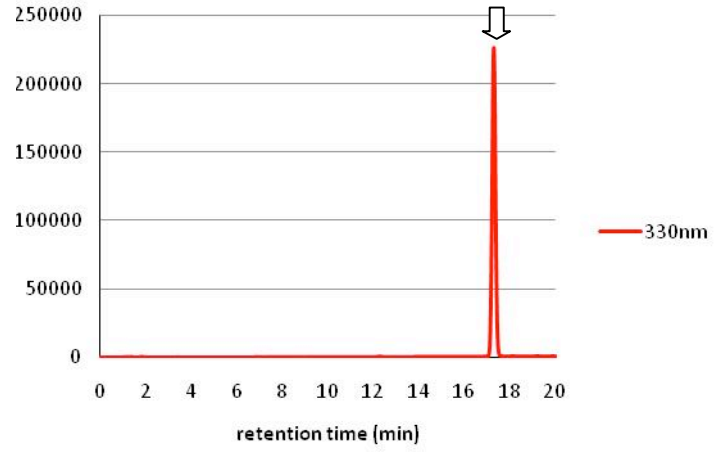
Table S2. Formation of NO_2^-/NO_3^- from **1** (10μM) upon photoirradiation (15 min)

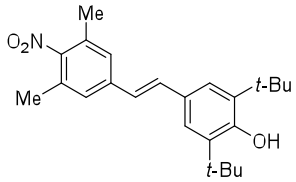
$[NO_2^-]$ (μM)	$[NO_3^-]$ (μM)	$[NO_2^-]+[NO_3^-]$ (μM)
0.99±0.11	1.13±0.17	2.16±0.13

a)


120000
100000
80000
60000
40000
20000
0
0 2 4 6 8 10 12 14 16 18 20
retention time (min)
254nm
286nm
330nm
446nm

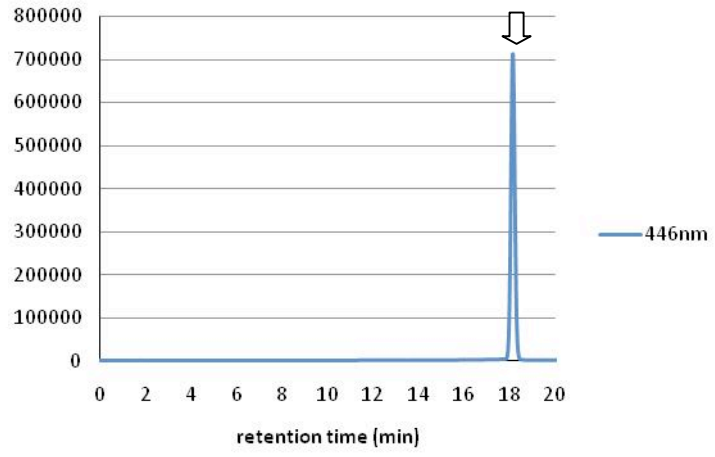
b)

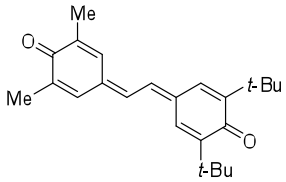

250000
200000
150000
100000
50000
0
0 2 4 6 8 10 12 14 16 18 20
retention time (min)
330nm


Me
O2N
Me
t-Bu
OH
t-Bu

1

c)


800000
700000
600000
500000
400000
300000
200000
100000
0
0 2 4 6 8 10 12 14 16 18 20
retention time (min)
446nm


Me
O
Me
t-Bu
O
t-Bu

2

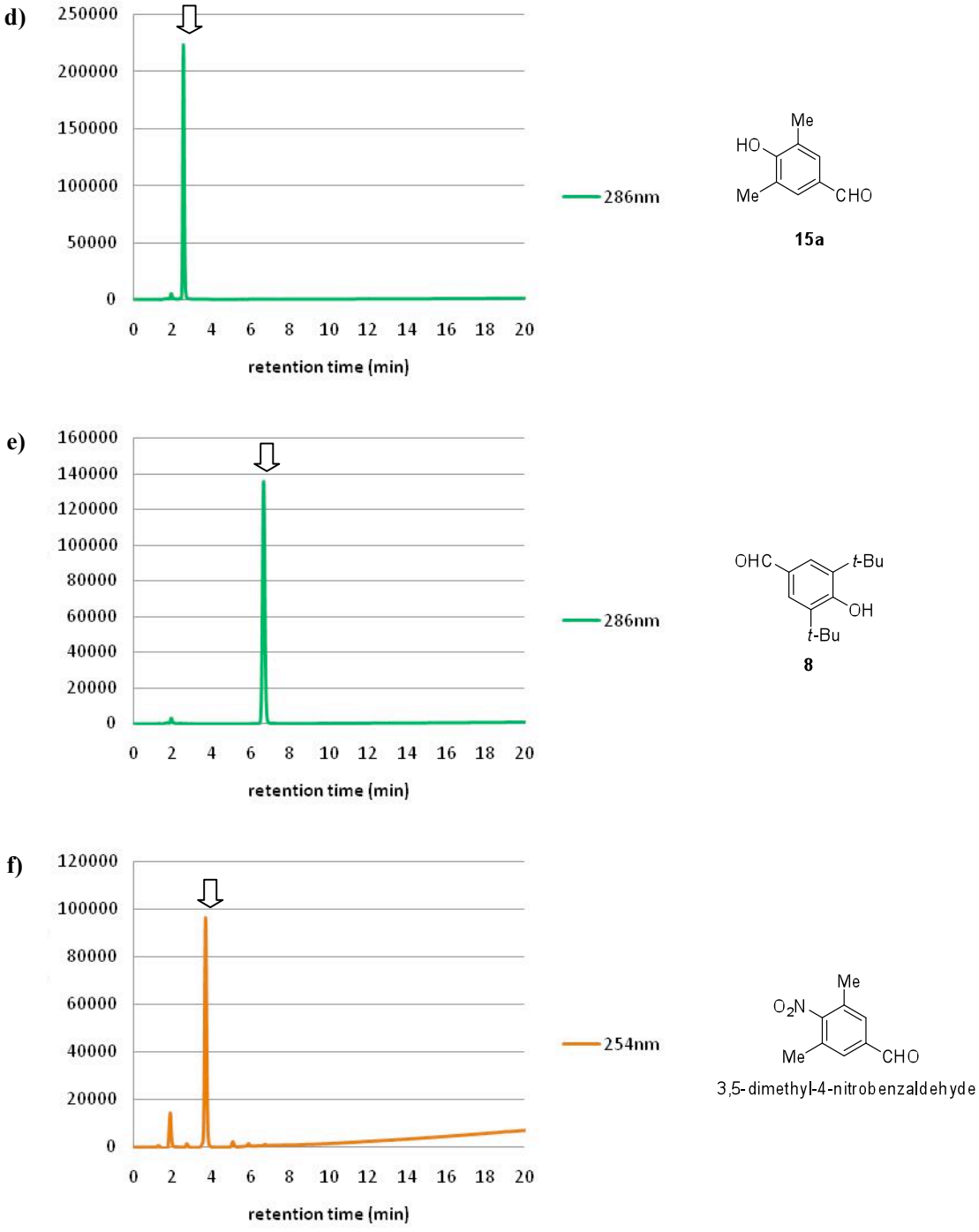


Figure S2. Detection of photo-decomposition products of **1** by means of reverse-phase HPLC: a) HPLC chromatogram of a photoirradiated solution of **1** (100 µM); b-f) HPLC chromatograms of authentic solutions (100 µM) of various compounds: b) **1**, c) **2**, d) **15a**, e) **8**, f) 3,5-dimethyl-4-nitrobenzene.