Synthesis of 5(6*H*)-Phenanthridones Using Diels–Alder Reaction of 3-Nitro-2(1*H*)-quinolones Acting as Dienophiles

Reiko FUJITA,* Toshiteru YOSHISUJI, Sota WAKAYANAGI, Hideaki WAKAMATSU, and Hisao MATSUZAKI

Tohoku Pharmaceutical University; 4–4–1 Komatsushima, Aoba-ku, Sendai 981–8558, Japan.
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Diels–Alder reactions of 3-nitro-2(1*H*)-quinolones with 1,3-butadiene derivatives were carried out to give the phenanthridone derivatives under both atmospheric and high pressure conditions. Furthermore, the reactivity of 3-substituted 2(1*H*)-quinolones acting as a dienophile with 2,3-dimethyl-1,3-butadiene was examined using molecular orbital (MO) calculation.

Key words 3-nitro-2(1*H*)-quinolone; Diels–Alder reaction; 6(5*H*)-phenanthridone; 1-methoxy-1,3-butadiene; 2,3-dimethoxy-1,3-butadiene; molecular orbital (MO) calculation

2(1*H*)-Quinolones are classified as aromatic heterocycles. With regard to reactions of 2(1*H*)-quinolones, substitution reactions[1—8] have been widely reported, but little attention has been focused on addition reactions. Diels–Alder (DA) reaction of 2(1*H*)-quinolones with diene afforded the phenanthridones in one pot. Recently, Weltin verified the ability of the 6(5*H*)-phenanthridones to inhibit poly(ADP-ribose)-polymerase (PARP) activity in lymphoma cells.[9—12] Furthermore, Cheng reported that 8,9-dimethoxyphenanthridinium salts (**A**, Chart 1) possess activity against leukemias P388.[13] We reported the synthesis of functionalized phenanthridones by novel DA reaction of 1-methyl-2(1*H*)-quinolones having an electron-withdrawing group (such as methoxycarbonyl, acetyl, cyano) at the 4- or 3-position that acts as a dienophlie.[14—17] It is well known that the nitro group function as a leaving group and a strong electron-withdrawing group. Herein, we report the synthesis of 6(5*H*)-phenanthridones by DA reaction of 3-nitro-2(1*H*)-quinolones under atmospheric and high pressure (AP and HP) conditions, and we investigate of the reactivity of the 2(1*H*)-quinolones using molecular orbital (MO) calculation.

DA Reaction Firstly, DA reactions of 3-nitro- (**1a**) and 3,6-dinitro-1-methyl-2(1*H*)-quinolones (**1b**)[18,19] with 1,3-butadienes (**2a**, **b**) were investigated under AP and HP conditions, as shown in Table 1 and Chart 1. DA reactions of **1a**, **b** with 1-methoxy-1,3-butadiene (**2a**) were carried out at 180 °C for 5 d in *o*-xylene (entries 1, 4), and gave 6(5*H*)-phenanthridones (**3a**,[20] 83%; **3b**, 68%), respectively. The same reaction of **3a** at 160 °C for 3 d (entry 2), also afforded **3a** (63%). On the other hand, DA reaction of **1a** with **2a** was performed under HP conditions (10 kbar) at 90 °C for 2 d (entry 3), and gave *endo*-DA adduct (**4a**, 57%) and *exo*-DA adduct (**4b**, 20%), respectively. Heating of **4a**, **b** at 180 °C in sealed tube produced **3a** (67%, 64%, respetively) aromatized by elimination of hydrogen and nitrogen dioxide (HNO_2), followed by release of MeOH. These facts indicated that **3a**, **b** resulted from release of HNO_2 and MeOH of corresponding DA adducts (such as **4a**) under AP conditions. Furthermore, DA reactions of **1a** with 2,3-dimethoxy-1,3-butadiene (**2b**) at 180 °C under AP condition gave 1-methyl-8,9-dimethoxy-6(5*H*)-phenanthridone (**6a**[3]; 31%, 45%, entries 5, 6) which was the synthetic intermediate for **A** possessing a bioactivity. DA reactions of **1b** with **2b** at 180 °C afforded 1-methyl-8,9-dimethoxy-2-nitro-6(5*H*)-phenanthridone (**6b**; 17%, 13%, entries 7, 8) in poor yields. But, DA reactions of **1a**, **b** with **2b** under HP condition (10 kbar) at 90 °C for 2 d afforded DA adducts (**5a**, 57%; **5b**, 55%, entries 9, 10) in reasonable yields. Heating of **5a**, **b** at 180 °C produced **6a** (48%) and **6b** (40%) aromatized by release of HNO_2, followed by dehydrogenation, respectively. The stereochemistries of the group at C-7 in **4a**, **b** were determined by nuclear Overhauser effect (NOE) measurement of ^{1}H-NMR spectra. The spectrum of **4a** indicated a correlation between H-7 and H-10a, but no such correlation was seen in the **4b** spectrum. Consequently, the stereochemistries between the methoxy group and H-10a were confirmed as *trans* in **4a** and *cis* in **4b**.

Next, DA reactions of 3-nitro-2(1*H*)-quinolone (**1c**)[18,19] with **2a**, **b**, 1-methoxy-3-silyloxy-1,3-butadienes (**2c**, **d**) and 2,3-disubstituted 1,3-butadienes (**2b**, **e**) were investigated under AP conditions, as shown in Table 2 and Chart 2. DA reactions of **1c** with **2a** were carried out in 1,2-dimethoxyethane (DME) and tetrahydrofurane (THF) since **1c** was insoluble in *o*-xylene. DA reaction of **1c** with **2a** at 180 °C for 1 d in DME (entry 1) gave 6(5*H*)-phenanthridone (**7**,[21,22] 52%) possing bioactivity and *exo*-DA adduct (**8**, 33%) an excellent yield. The same reaction for 5 d in DME (entry 2) afforded **7** (50%) and **8** (30%), and in THF for 3 d (entry 3), afforded **7** (44%) and **8** (28%). Heating of **8** at 180 °C in sealed tube produced **7** (8% only) aromatized by elimination of HNO_2 and MeOH. Based on the above facts, it can be presumed that **7** mostly result by aromatization from corresponding *endo*-DA adduct. DA reaction of **1c** with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (**2c**) at 160 °C for 3 d in DME (entry 4) gave 9-hydroxy-6(5*H*)-phenanthridone (**9**, 43%) and 9-methoxy-6(5*H*)-phenanthridone (**11**,[23] 7%), and the same reaction at 180 °C (entry 5) gave **9** (57%) and **11** (9%) in good yield. Similerly, DA reaction of **1c** with 1-methoxy-3-*t*-butyldimethylsilyloxy-1,3-butadiene (**2d**) at 180 °C for 3 d in DME (entry 6) afforded **9** (56%), **11** (1%) and 9-*t*-butyldimethylsilyloxy-6(5*H*)-phenanthridone (**10**, 38%) in quantitative yield. Treatment of **10** with tetra-*n*-butylammonium fluoride (TBAF) in THF at 30 °C for 6 h produced **9** in 80% yield. Moreover, DA reaction of **1c** with **2b** at 160 °C for 5 d (entry 7) afforded 8,9-dimethoxy-6(5*H*)-phenanthridone (**13a**,[24] 20%) and 8-methoxy-6(5*H*)-phenanthridone (**14**,[23] 30%). The same reactions at 180 °C for 3 or 5 d (entries 8, 9) also gave **13a** (22%, 33%) and **14** (16%,

* To whom correspondence should be addressed. e-mail: refujita@tohoku-pharm.ac.jp

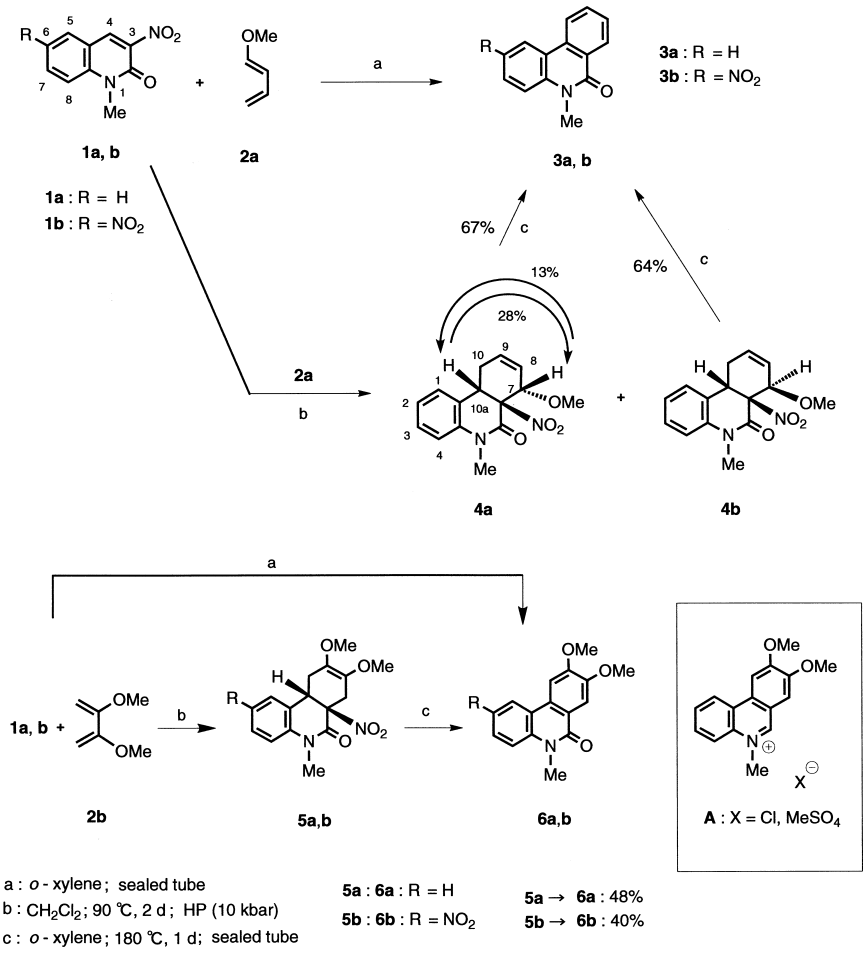

Chart 1

Table 1. Diels–Alder Reactions of **1a**, **b** with **2a**, **b**

Entry	Quinolone	Diene	Temp. (°C)	Time (d)	Solvent	Pressure (kbar)	Product	Yield (%)
1	**1a**	**2a**	180	5	*o*-Xylene	Atmospheric	**3a**	83
2	**1a**	**2a**	180	3	*o*-Xylene	Atmospheric	**3a**	63
3	**1a**	**2a**	90	2	CH_2Cl_2	10	**4a**	57
							4b	20
4	**1b**	**2a**	180	5	*o*-Xylene	Atmospheric	**3b**	68
5	**1a**	**2b**	180	5	*o*-Xylene	Atmospheric	**6a**	31
6	**1a**	**2b**	180	3	*o*-Xylene	Atmospheric	**6a**	45
7	**1b**	**2b**	180	5	*o*-Xylene	Atmospheric	**6b**	17
8	**1b**	**2b**	180	3	*o*-Xylene	Atmospheric	**6b**	13
9	**1a**	**2b**	90	2	CH_2Cl_2	10	**5a**	57
10	**1b**	**2b**	90	2	CH_2Cl_2	10	**6b**	55

8%), respectively. DA reaction of **1c** with 2,3-dimethyl-1,3-butadiene (**2e**) at 180 °C for 3 d (entry 10) afforded only 8,9-dimethyl-6(5*H*)-phenanthridone (**13b**,[25] 48%).

The stereochemistry of between the methoxy group at C-7 and H-10a in **8** was confirmed that since the methylation of **8** gave **4b**, that in **8** was also *cis*. The structures of **9**, **10**, **11** and **14** were determined as follows. Methylation of **9** and **11** produced a known compound (**12**)[26] bearing a methoxy group at the 9-position. Similarly, methylation of **14** also produced a known compound (**15**)[26] bearing a methoxy group at the 8-position. Consequently, the methoxy group in **9** and **11** occupied the 9-position, and that in **14** occupied at the 8-position. It was considered that **14** was drived from **13a** by elimination of HNO_2 and demethanolation. Desilylation of **10** gave **9**, so that the silyloxy group in **10** occupied the 9-position. It was assumed that methylation of **9** for production of **11** would be a source of DME.[27]

Yields of Adducts and Activation Energy We theoretically studied the reactivity of the DA reactions of 3-substituted and non-substituted quinolones (**1a**, **c**, **16a**, **b**, **18a**, **b**) with dimethylbutadiene (**2e**; Chart 3). We calculated activation energies (*Ea*) of the DA reactions listed in Table 3 using

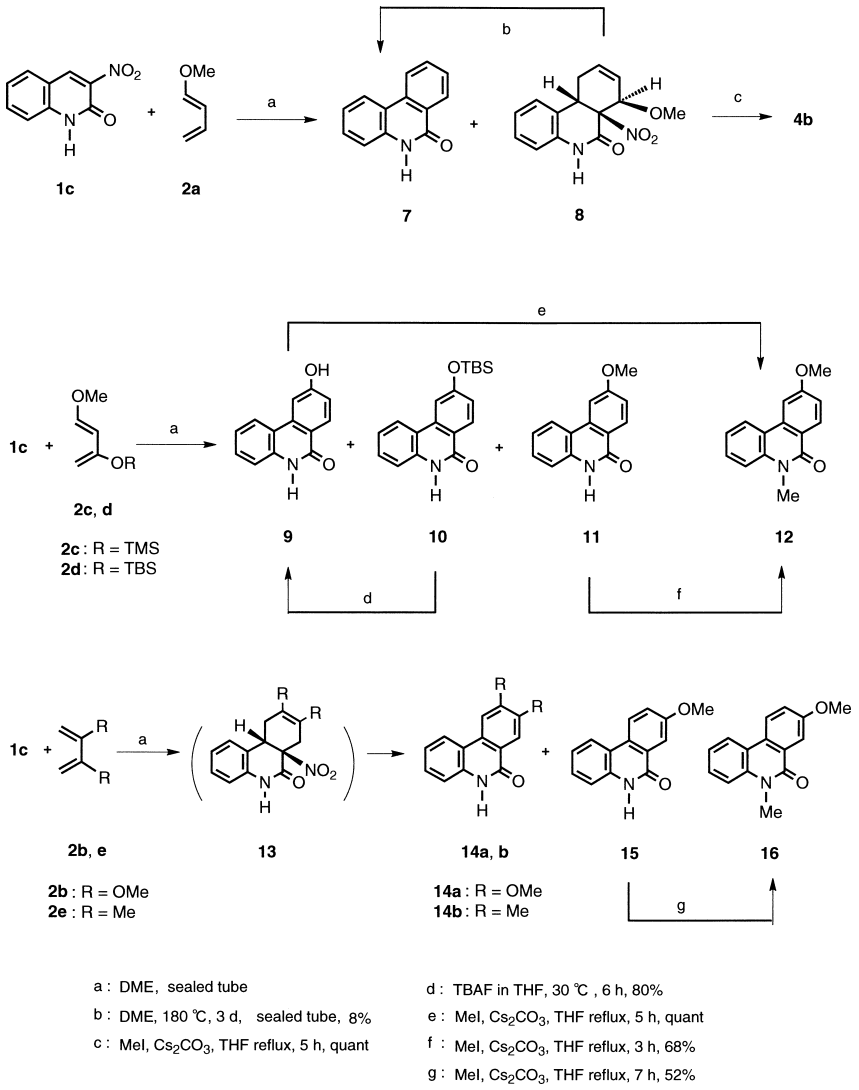

Chart 2

Table 2. Diels–Alder Reactions of **1c** with **2a**—**e** under the Atmospheric Conditions

Entry	Diene	Temp. (°C)	Time (d)	Solvent	Product No.	Yield (%)
1	**2a**	180	1	DME	**7**	52
					8	33
2	**2a**	180	5	DME	**7**	50
					8	30
3	**2a**	180	3	THF	**7**	44
					8	28
4	**2c**	160	3	DME	**9**	43
					11	7
5	**2c**	180	3	DME	**9**	57
					11	9
6	**2d**	180	3	DME	**9**	56
					10	38
					11	1
7	**2b**	160	5	DME	**14a**	20
					15	30
8	**2b**	180	3	DME	**14a**	22
					15	16
9	**2b**	180	5	DME	**14a**	33
					15	8
10	**2e**	180	3	DME	**14b**	48

Gaussian 98 at B3LYP/6-31G(d) level.[28] We searched and obtained the *endo*- and *exo*-type transition states (TS). Since the *exo*-type TS have lower energy than the *endo*-type in these DA reactions and the both TS's lead to the same product, we calculated *Ea* as a difference in energy between the *exo*-type TS and the initial state. The calculated values of *Ea*, the yields of adducts, and the SM recoveries are shown in Table 3. Since the fraction of side reactions is thought to be small from these data, we can regard the yield of adduct as an index of the reactivity. The yields of DA reactions of 3-substituted *N*-methylquinolones (**1a**, **16a**) are well correlated with the calculated values of *Ea*. The yields of DA reactions of non-substituted quinolones (**18a**, **b**) with **2e** were zero. They are consistent with the fact that the calculated values of *Ea* of these reactions are considerably larger than the others. The yields of the DA reactions of *NH*-quinolones (**1c**, **16b**) are smaller than those of *N*-methylquinolones (**1a**, **16a**), respectively. Whereas, the calculated values of *Ea* expect the reverse results. Nevertheless, *NH*-quinolones (**1c**, **16b**) cause a *keto–enol* tautomerization. We calculated the energies of the *keto*- and *enol*-type quinolones (**1c**, **16b**) at B3LYP/6-31++G (d, p) level. The obtained energies of *keto*-type

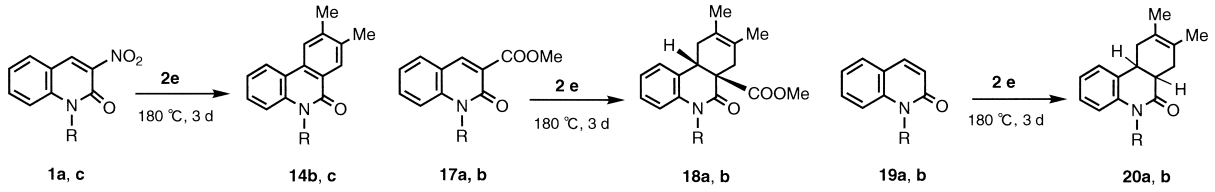

Chart 3

Table 3. Yields of Adducts and Activation Energies (*Ea*) Calculated Using Gaussian 98 at B3LYP/6-31G(d) Level

Quinolone	Group on the 3-position	R	*Ea* (kcal/mol)	Population[a)] (%)	Adduct	Yield (%)	SM recov. (%)
1a	NO_2	Me	20.41	—	**14c**	95[15)]	—
1c	NO_2	H	19.65	36	**14b**	48	32
17a	COOMe	Me	23.82	—	**18a**	40[15)]	51
17b	COOMe	H	23.33	41	**18b**	0	97
19a	H	Me	27.01	—	**20a**	0	96
19b	H	H	26.30	99	**20b**	0	97

a) Population of the *keto*-type quinolones calculated at B3LYP/6-31++G(d, p) level.

quinolones are 0.51 and 0.32 kcal/mol larger than those of *enol*-type of **1c** and **16b**, respectively. These differences in energy respectively correspond to the populations of *keto*-type of 36% and 41%, as shown in Table 3. We can presume that the lowered populations of *keto*-type quinolones caused the drop of reactivity of these DA reactions and leaded to small yields of adducts.

In conclusion, we prepared the desired phenanthridones using DA reactions of 3-nitro-2(1*H*)-quinolones with 1-methoxy-, 3-silyloxy- and 2,3-disubstituted 1,3-butadienes. We have also developed a methodology for phenanthridone synthesis. We can understand qualitatively the reactivity of DA reactions listed in Table 3 in terms of the activation energies and the population of *keto*-type quinolones.

Experimental

The following instruments were used to obtain physical data: Melting points, Yanaco micromelting point apparatus (values are uncorrected); IR spectra, Perkin Elmer ET-IR 1725X spectrometer; MS, JEOL JMN-DX 303/JMA-DA5000 spectrometer; NMR spectra, JNM-GSX 400 (^{1}H-NMR, 400 MHz; ^{13}C-NMR, 100 Hz), JNM-EX270 (^{1}H-NMR, 270 MHz; ^{13}C-NMR, 67.5 MHz), JEOL JNM-PMX 60SI spectrometer with tetra-methylsilane (TMS) as an internal standard; and elemental analysis, PERKINELMER 2400 CHN Elemental Analyzer. Chromatography was carried out under the following experimental conditions: column chromatography, Merk Kieselgel silica gel 60 (230—400 mesh); TLC, pre-coated TLC plates with $60F_{254}$ (2 mm, Merck).

Typical Procedure for DA Reactions of 1a, b with 2a a) A *o*-xylene solution (3 ml) of **1a** (204 mg, 1 mmol) and **2a** (420 mg, 5 mmol) was heated at 180 °C for 5 d in a sealed tube. The reaction mixture was concentrated *in vacuo*. The residue was subjected to chromatography on a silica gel column. The first fraction eluted with acetone–hexane (1 : 2) was evaporated to gave **3a**.[6)] b) Reactions of **1a**, **b** (1 mmol) with **2a** (5 mmol) were carried out under the conditions listed in Table 1 and products were purified as described above to gave **3a**, **b**. The respective yields of the above compounds are summarized in Table 1.

DA Reaction of 1a with 2a under HP Condition A mixture of **1a** (53 mg, 0.26 mmol) and **2a** (141 mg, 1 mmol) in dichloromethane (3 ml) was placed in a Teflon tube. The tube was placed in a high pressure reactor and pressurized to 10 kbar, followed by heating at 90 °C for 2 d. Pressure was released and the reaction mixture was concentrated *in vavuo*. The residue was subjected to chromatography on a silica gel column. The first fraction eluted with acetone–hexane (1 : 2) was evaporated to give 5,6,6a,7,8,10a-hexahydro-7β-methoxy-5-methyl-*cis*-6a-nitro-6(5*H*)-phenanthridone (**4b**). The second fraction was evaporated to give 5,6,6a,7,8,10a-hexahydro-7α-methoxy-5-methyl-*cis*-6a-nitro-6(5*H*)-phenanthridone (**4a**). The yields of the above compounds are summarized in Table 1.

Heating of 4a, b a) The solution of **4a** (43.2 mg, 0.15 mmol) in 3 ml *o*-xylene was heated at 180 °C for 1 d and then concentrated *in vacuo*. The residue was purified by chromatography on a silicagel. The fraction eluted with hexane–ethyl acetate (1 : 1) was evaporated to give **3a** (21 mg, 67%). b) Heating of **4b** (15 mg, 0.052 mmol) was carried out under the same condition and the product was purified by preparative TLC over silicagel with hexane–ethyl acetate (1 : 1) to give **3a** (6 mg, 64%).

Typical Procedure for DA Reaction of 1a, b with 2b a) A *o*-xylene solution (3 ml) of **1a** (204 mg, 1 mmol) and **2b** (575 mg, 5 mmol) was heated at 180 °C for 3 d in a sealed tube. The reaction mixture was concentrated *in vacuo*, and the residue was subjected to chromatography on a silica gel column. The first fraction eluted with acetone–hexane (1 : 1) was evaporated to gave **6a**. b) Reactions of **1a**, **b** (1 mmol) with **2b** (5 mmol) were carried out under the conditions listed in Table 1 and products were purified as described above to give **6a**, **b**. The respective yields of the above compounds are summarized in Table 1.

DA Reaction of 1a with 2b under HP Condition A mixture of **1a** (57 mg, 0.28 mmol) and **2b** (141 mg, 1 mmol) in dichloromethane (3 ml) was placed in a Teflon tube. The tube was placed in a high pressure reactor and pressurized to 10 kbar, followed by heating at 90 °C for 2 d. Pressure was released and the reaction mixture was concentrated *in vavuo*. The residue was subjected to chromatography on a silica gel column to give 5,6,6a,7,8,10a-hexahydro-8,9-dimethoxy-5-methyl-*cis*-6a-nitro-6(5*H*)-phenanthridone (**5a**).

Heating of 5a, b a) The solution of **5a** (5 mg, 0.015 mmol) in 1 ml *o*-xylene was heated at 180 °C for 1 d and then concentrated *in vacuo*. The residue was purified by preparative TLC over silicagel with hexane–ethyl acetate (1 : 1) to give **6a** (2 mg, 48%). b) Heating of **5b** (15 mg, 0.041 mmol) was carried out under the same condition and product was purified as described above to give **6b** (6 mg, 40%).

Typical Procedure for DA Reaction of 1c with 2a a) A DME solution (1.5 ml) of **1c** (50 ml, 0.26 mmol) and **2a** (0.13 ml, 1.315 mmol) was heated at 180 °C for 3 d in a sealed tube. The reaction mixture was concentrated *in vacuo*, and the residue was subjected to chromatography on a silica gel column. The fraction eluted with ethyl acetate was evaporated and the residue was added $CHCl_3$ (20 ml). The $CHCl_3$ layer was washed with saturated aqueous NaCl and concentrated *in vacuo*. The residue was subjected to chromatography on a silica gel column. The first fraction eluted with acetone–hexane (1 : 2) was evaporated to give 5,6,6a,7,8,10a-hexahydro-7-methoxy-*cis*-6a-nitro-6(5*H*)-phenanthridone (**8**). The second fraction was evaporated to give **7**. The yields of **8** are summarized in Table 2.

Heating of 8 a) The solution of **8** (50 mg, 0.183 mmol) in 1.5 ml DME was heated at 180 °C for 3 d and then concentrated *in vacuo*. The residue was purified by preparative TLC over silicagel with hexane–ethyl acetate (1 : 1) to give **7** (3 mg, 8%, *Rf*=0.35) and the recovery of **8** (38 mg, 76%, *Rf*=0.45).

Methylation of 8 To a suspention of cesium carbonate (470 mg, 1.45 mmol) and **8** (80 mg, 0.29 mmol) in THF (5.4 ml) was added MeI (0.05 ml, 0.87 mmol)] at room temperature under N_2. The mixture was refluxed for 5 h. The reaction mixture was concentrated *in vacuo*, quenched with H_2O (8 ml) and extacted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl and dried over $MgSO_4$. The ethyl acetate was evapolated *in vacuo* and the residue was chromatographed on a column of silica gel. The solvent of first fraction eluted with ethyl acetate–hexane (1 : 2) was evaporated to give **4b** (84 mg, quant).

Typical Procedure for DA Reaction of 1c with 2c, d a) A solution of **1c** (150 mg, 0.789 mmol) and **2c** (0.75 ml, 3.945 mmol) in DME (4.5 ml) was heated at 180 °C for 3 d in a sealed tube. The reaction mixture was concentrated *in vacuo* and diluted with chloroform (20 ml). To the reaction mixture, TFA (0.75 ml) was added with stirring at room temperature for 20 min and concentrated *in vacuo*. The residue was chromatographed on a column of silica gel. The solvent of first fraction eluted with ethyl acetate–hexane (2 : 1) was evaporated to give **11**. The solvent of second fraction was evaporated to give **9**. b) A solution of **1c** (150 mg, 0.789 mmol) and **2d** (0.94 ml, 3.95 mmol) in DME (4.5 ml) was heated at 180 °C for 3 d in a sealed tube. The reaction mixture was concentrated *in vacuo* and diluted with chloroform (20 ml). To the reaction mixture, TFA (0.75 ml) was added with stirring at room temperature for 20 min and concentrated *in vacuo*. The residue was chromatographed on a column of silica gel. The solvent of first fraction eluted with ethyl acetate–hexane (1 : 1) was evaporated to give **10**. The solvent of second fraction was evaporated to give **11**. The solvent of third fraction was evaporated to give **9**.

Treatment of 10 with TBAF To a solution of **10** (15 mg, 0.047 mmol) in THF (1 ml) was added 1 mol/THF TBAF (0.14 ml, 0.14 mmol) and the reaction solution was stirred at 30 °C for 6 h. The reaction mixture was evaporated in *in vacuo*. The residue was chromatographed on a column of silicagel. The soluvent of first fraction with eluted acetone–hexane (1 : 1) was evaporated in *in vacuo* to give **9** (8 mg, 80%).

Methylation of 9 To a suspention of cesium carbonate (115 mg, 0.335 mmol) and **9** (15 mg, 0.071 mmol) in THF (6 ml) was added MeI (0.017 ml, 0.284 mmol)] at room temperature under N_2. The mixture was refluxed for 5 h. The reaction mixture was concentrated *in vacuo,* quenched with H_2O (6 ml) and extacted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl and dried over $MgSO_4$. The ethyl acetate was evapolated *in vacuo* and the residue was chromatographed on a column of silica gel. The solvent of first fraction eluted with ethyl acetate–hexane (1 : 2) was evaporated to give **12** (17 mg, quant).

Methylation of 11 To a suspention of cesium carbonate (114 mg, 0.335 mmol) and **11** (16 mg, 0.07 mmol) in THF (6 ml) was added MeI (0.013 ml, 0.21 mmol)] at room temperature under N_2. The mixture was refluxed for 3 h. The reaction mixture was concentrated *in vacuo*, quenched with H_2O (6 ml) and extacted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl and dried over $MgSO_4$. The ethyl acetate was evapolated *in vacuo* and the residue was chromatographed on a column of silica gel. The solvent of first fraction eluted with ethyl acetate–hexane (1 : 2) was evaporated to give **12** (11 mg, 65%).

Typical Procedure for DA Reaction of 1c with 2b, e a) A DME solution (1.5 ml) of **1c** (50 mg, 0.26 mmol) and **2b** (0.16 ml, 1.315 mmol) was heated at 180 °C for 3 d in a sealed tube. The reaction mixture was concentrated *in vacuo*, and the residue was subjected to chromatography on a silica gel column. The fraction eluted with ethyl acetate was evaporated and the residue was added $CHCl_3$ (20 ml). The $CHCl_3$ layer was washed with saturated aqueous NaCl and concentrated *in vacuo*. The residue was subjected to chromatography on a silica gel column. The first fraction eluted with acetone–hexane (1 : 2) was evaporated to gave **14**. The second fraction was evaporated to give **1c** (10 mg, 10%). The third fraction was evaporated to gave **13a**. The respective yields of the above compounds are summarized in Table 2. b) Reactions of **1c** (0.26 mmol) with **2e** (5 mmol) was carried out under the conditions listed in Table 2 and products were purified as described above to gave **13b** and the recover of **1c**.

Methylation of 14 To a suspention of cesium carbonate (144 mg, 0.445 mmol) and **9** (20 mg, 0.089 mmol) in THF (6 ml) was added MeI (0.016 ml, 0.269 mmol) at room temperature under N_2. The mixture was refluxed for 7 h. The reaction mixture was concentrated *in vacuo*, quenched with H_2O (8 ml) and extacted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl and dried over $MgSO_4$. The ethyl acetate was evapolated *in vacuo* and the residue was chromatographed on a column of silica gel. The solvent of first fraction eluted with ethyl acetate–hexane (1 : 1) was evaporated to give **15** (11 mg, 54%). The solvent of second fraction was evaporated to recover **14** (9 mg, 40%).

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