Cycloadditions of 1-Substituted 1,3-Butadienes with 4- or 3-Substituted 2(1*H*)-Quinolones Acting as Dienophiles

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Cycloadditions of 1,3-butadiene derivatives having an electron-rich group at the 1-position with 4- or 3-substituted 2(1*H*)-quinolones were carried out to give the richly functionalized phenanthridines under both atmospheric and high pressure conditions. Furthermore, the reactivity of 4- or 3-substituted 2(1*H*)-quinolones acting as a dienophile with 1-substituted dienes was examined using MO calculation.

Key words 4-substituted 2(1*H*)-quinolone; cycloaddition; phenanthridine; MO calculation; high pressure; electron-withdrawing group

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 reaction of 2(1*H*)-quinolone with diene afforded a phenanthridine derivative.[9] Because numerous Amaryllidaceae alkaloids contain phenanthridine skeletons,[10—12] functionalized phenanthridines would be potentially valuable synthetic intermediates, and may possess novel pharmacological activities.[10—12] We recently reported phenanthridine synthesis by cycloaddition of 1-methyl-2(1*H*)-quinolones having an electron-withdrawing group at the 4- or 3-position that acts as a dienophlie towards 2-, 2,3-substituted dienes as well as Danishefsky's diene.[13—16] However, there are no reports regarding cycloaddition of 1-substituted 1,3-butadienes with 1-methyl-2(1*H*)-quinolones. Herein, we report the synthesis of phenanthridines richly functionalized by cycloaddition of 1,3-butadienes bearing methoxy or equivalent groups at the 1- or 1,4-positions with 1-methyl-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 MO calculation. The HP strategy has proven extremely useful in surmounting the energy barrier imposed by the steric and electronic interactions in cycloaddition.[17,18]

Cycloaddition Cycloaddition of 1-methyl-2(1*H*)-quinolones **1**—**4** having methoxycarbonyl,[19,20] or cyano[21—24] groups at the 4- or 3-position with 1- or 1,4- substituted 1,3-butadienes [**5** (OMe), **6** ($OSiMe_3$), **7** (OCOMe), **8** $(OCOMe)_2$] was investigated under AP conditions, as shown in Table 1 and Chart 1. Cycloaddition of 1-methoxydiene **5** with quinolone **1** having a methoxycarbonyl group at the 4-position was carried out at 180 °C for 6 d (entry 1), and regioselectively gave *cis-endo*-adduct (**9a**, 67%) and *cis-exo*-adduct (**10a**, 21%) in accordance with the Alder–Stein rule (*cis*-principle)[25] at an excellent yield. The same reaction at 160 °C for 4 or 6 d (entries 2, 3), also afforded *cis*-adducts (**9a**, 14%; **10a**, 59% and **9a**, 21%; **10a**, 15%, respectively). The reaction at 200 °C (entry 4) also gave adducts (**9a**, 38%; **10a**, 11%). These results suggest that while cycloaddition at 180 °C favored the *endo*-addition pathway to **9a**, that at 160 °C favored the *exo*-addition pathway to **10a**. Cycloaddition of **5** with quinolone **2** bearing a cyano group at the 4-position at 180 °C (entries 5, 6) regioselectively gave *cis-endo*-adduct (**9b**, 27%, 32%) and *cis-exo*-adduct (**10b**, 30%, 24%) in reasonable yields. Moreover, cycloaddition of 1-trimethylsiloxydiene **6** with **1** proceeded smoothly at 160 and 180 °C for 6 d (entries 7, 8), and the reaction mixtures were treated with trifluoroacetic acid (TFA) to regioselectively give the corresponding *cis-endo*-adduct (**9c**, 39%, 39%) and *cis-exo*-adduct (**10c**, 29%, 29%) in good yields. Similarly, cycloaddition of **6** with **2** (entries 9, 10) afforded *cis-endo*-adduct (**9d**, 19%, 20%) and *cis-exo*-adduct (**10d**, 41%, 34%) in reasonable yields. The reactions of mono- and diacetoxydienes **7**, **8** were also investigated. Cycloaddition of **7** with **1** at 160 and 180 °C gave only a single *cis-endo*-adduct (**9e**, 30%; entry 11 and **9e**, 30%; entry 12), whereas cycloaddition of **7** with **2** (entries 13, 14) afforded several *cis-endo*-adduct (**9f**, 3%, 7%) and *cis-exo*-adduct (**10f**, 11%, 12%). Reaction of **8** with **1** (entries 15, 16) proceeded to stereoselectively afford *cis-endo*-adduct (**9g**, 38%, 10%, respectively). Cycloaddition of 1-methoxydiene **5** with quinolone **3** having a methoxycarbonyl group at the 3-position at 180 and 160 °C for 6 d (entries 17, 18) was then performed and gave *cis-endo*-adducts (**11a**, 14%, 3%) and (**12a**, 11%, 14%), respectively. Reactions of 1-trimethylsiloxydiene **6** with **3** proceeded but gave poor yields and the corresponding adducts were not purified by TLC and/or column chromatography. Cycloaddition of **5** and **6** with quinolone **4** bearing a cyano group at 3-position afforded only *cis-exo*-adducts (**12b**, 20%, 25%; entries 19, 20; **12d**, 5%, 6%; entries 23, 24). Comparison of yields of the adducts produced from **1** and **2** with **3** and **4** revealed that 4-substituted quinolones afforded satisfactory yields, and cycloaddition of **1** with **5** and **6** gave the adducts in good yields.

Cycloaddition of **1**—**4** with **5**—**8** was then performed under HP conditions (10 kbar) at 90 °C (Table 2). Reactions of **1**—**4** with **5** (entries 1—4) afforded *cis-endo*-adducts (**9a**, 14%; **9b**, 29%; **11a**, 14%; **11b**, 0%) and *cis-exo*-adducts (**10a**, 20%; **10b**, 31%; **12a**, 23%; **12b**, 41%), respectively. TFA was added to the reaction mixtures of **1** and **2** with **6** (entries 5, 6) to give the corresponding *cis-endo*-adducts (**9c**, 25%; **9d**, 22%, respectively) and *cis-exo*-adducts (**10c**, 49%; **10d**, 33%) in good yields. Cycloaddition of **1** and **2** with **7** afforded *cis-endo*-adduct (**9e**, 53%; entry 7) and *cis-exo*-adduct (**10f**, 23%; entry 8). Reaction of **1** with **8** gave *cis-endo*-adduct (**9g**, 20%; entry 9). Consequently, comparison of the adduct yields produced under AP conditions with

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Table 1. Cycloadditions of **1**—**4** with **5**—**8**

Entry	Quinolone No.	Diene No.	Temp. (°C)	Time (d)	Work up (r.t.)	Product No.	Yield (%)	Product No.	Yield (%)
1	**1**	**5**	180	6	—	**9a**	67	**10a**	21
2	**1**	**5**	160	4	—	**9a**	14	**10a**	59
3	**1**	**5**	160	6	—	**9a**	21	**10a**	15
4	**1**	**5**	200	6	—	**9a**	38	**10a**	11
5	**2**	**5**	180	3	—	**9b**	27	**10b**	30
6	**2**	**5**	180	6	—	**9b**	32	**10b**	24
7	**1**	**6**	160	6	TFA	**9c**	39	**10c**	29
8	**1**	**6**	180	6	TFA	**9c**	39	**10c**	29
9	**2**	**6**	160	6	TFA	**9d**	19	**10d**	41
10	**2**	**6**	180	6	TFA	**9d**	20	**10d**	34
11	**1**	**7**	160	6	—	**9e**	30	**10e**	0
12	**1**	**7**	180	6	—	**9e**	30	**10e**	0
13	**2**	**7**	160	6	—	**9f**	3	**10f**	11
14	**2**	**7**	180	6	—	**9f**	7	**10f**	12
15	**1**	**8**	160	6	—	**9g**	38	**10g**	0
16	**1**	**8**	180	6	—	**9g**	10	**10g**	0
17	**3**	**5**	160	6	—	**11a**	14	**12a**	11
18	**3**	**5**	180	6	—	**11a**	3	**12a**	14
19	**4**	**5**	160	6	—	**11b**	0	**12b**	20
20	**4**	**5**	180	6	—	**11b**	0	**12b**	25
21	**3**	**6**	160	6	TFA	**11c**[a)]		**12c**[a)]	
22	**3**	**6**	180	6	TFA	**11c**[a)]		**12c**[a)]	
23	**4**	**6**	160	6	TFA	**11d**	0	**12d**	5
24	**4**	**6**	180	6	TFA	**11d**	0	**12d**	6

a) The mixtures of **11c** and **12c** were not purified by column or thin layer chromatographies and were in poor yields.

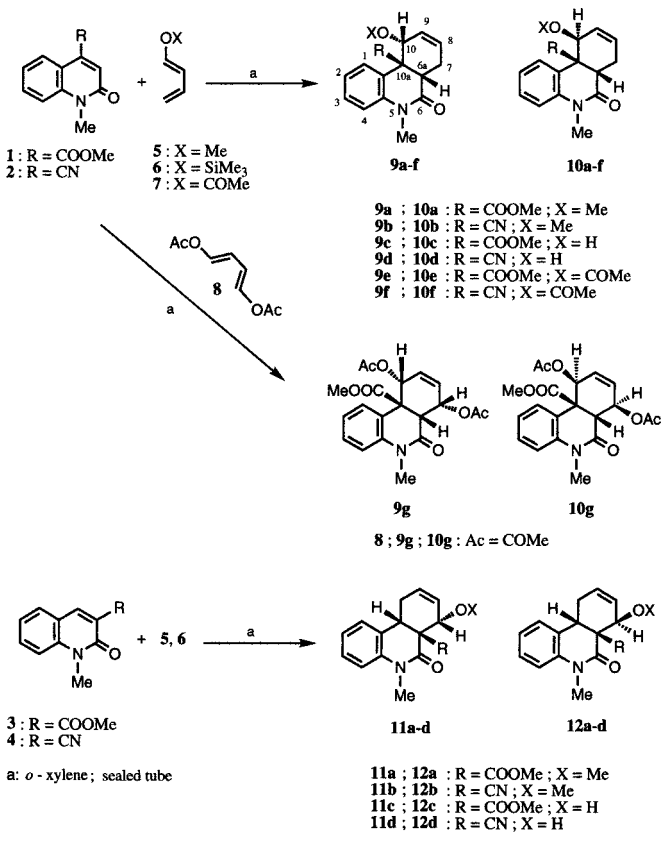

Chart 1

those formed under HP conditions revealed that HP-cycloaddition resulted in higher yields (Table 2), except for reaction of 1-methoxydiene **5** with **1**, which gave an excellent yield [total yield of adducts (**9a**, **10a**), 88%].

The stereochemistry of the ring junctures in **9a**—**g**, **10a**—**f**, **11a** as well as **12a**, **b**, and **d** were investigated. We previously reported that cycloaddition of 2(1*H*)-quinolones with 2,3-dimethyl-1,3-butadiene or Danishefsky's diene gave only *cis*-adducts, and the stereochemistry of the ring junctures in the adducts (**A**, **B**) were determined by X-ray crystallography (Fig. 1). The signals (δ 3.04—3.41) in the ^{1}H-NMR spectra due to H-6a in the *cis*-adducts (**C**) were observed at lower magnetic fields than those (δ 2.56—2.71) in the corresponding *trans*-adducts (**D**) formed by isomerization of the *cis*-adducts using a base (Fig. 1).[13—16] Signals due to H-6a in **9a**—**g** and **10a**—**f** appeared at δ 3.10—3.82. These results confirmed *cis* stereochemistry in the ring junctures of **9a**—**g**, and **10a**—**f**. Signals due to H-10a in the *cis*-adducts (**E**) were located at δ 3.47—3.92, and those due to H-10a in **11a** and **12a**, **b** and **d** appeared at δ 3.50—3.61. From the above data, **11a** and **12a**, **b** and **d** were assumed to have *cis* stereochemistry. Moreover, the stereochemistry of the groups at C-10 in **9a**—**g**, and **10a**—**f** as well as the groups at C-7 in **11a** and **12a**, **b** and **d** were determined by nuclear Overhauser effect (NOE) measurement of ^{1}H-NMR spectra. The spectrum of **9a** indicated a correlation between H-10 and H-6a, but no such correlation was seen in the **10a** spectrum. Consequently, the stereochemistry between the methoxy group and H-6a was confirmed as *trans* in **9a** and *cis* in **10a**. Similarly, the spectra of **9b**—**f** demonstrated a correlation between H-10 and H-6a, and those of **10b**—**f** did not show a correlation. The stereochemistry between the groups at C-10 and H-6a were confirmed as *trans* in **9b**—**f** and *cis* in **10b**—**f**. In contrast, the spectrum of **11a** indicated a correlation between H-7 and H-10a, but those of **12a** and **d** did not show a correlation. Therefore, the stereochemistry between the groups at C-7 and H-10a were confirmed as *trans* in **11a** and *cis* in **12a** and **d**. Furthermore, based on the correlations between H-7, 10 and H-6a in the **9g** spectrum, the stereochemistry between

Table 2. Cycloadditions of **1**—**4** with **5**—**8** under the Condition of High Pressure

Entry	Quinolone No.	Diene No.	Temp. (°C)	Time (d)	Pressure (kbar)	Work up (r.t.)	Product No.	Yield (%)	Product No.	Yields (%)
1	**1**	**5**	90	2	10	—	**9a**	14	**10a**	20
2	**2**	**5**	90	2	10	—	**9b**	29	**10b**	31
3	**3**	**5**	90	2	10	—	**11a**	14	**12a**	23
4	**4**	**5**	90	2	10	—	**11b**	0	**12b**	41
5	**1**	**6**	90	2	10	TFA	**9c**	25	**10c**	49
6	**2**	**6**	90	2	10	TFA	**9d**	22	**10d**	33
7	**1**	**7**	90	2	10	—	**9e**	53	**10e**	0
8	**2**	**7**	90	2	10	—	**9f**	0	**10f**	23
9	**1**	**8**	90	2	10	—	**9g**	20	**10g**	—

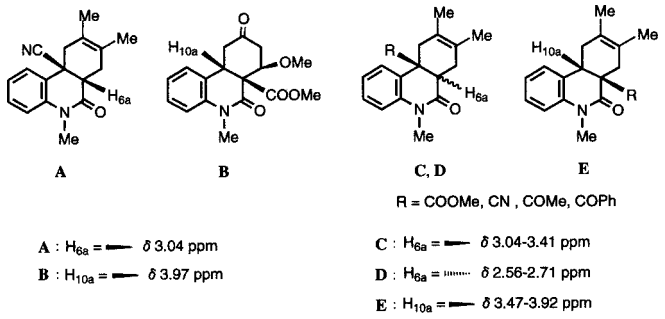

Fig. 1

the two acetoxy groups and H-6a in **9g** was confirmed as *trans*.

***Endo-* and *Exo*-Selectivity** In the present experiments, both *endo-* and *exo*-adducts were produced by cycloaddition of **1**—**4** with **6**—**8** (Table 1). We theoretically study the *endo-*/*exo*-selectivity of the cycloaddition reactions listed in Table 3. We optimized the structures of the initial states and the transition states (TS) using the AM1 method[26] and calculated the activation energy (*Ea*) of each reactions as the difference in energy between the TS and initial state. The optimized structures of the TS on cycloaddition of **1** and **3** with **5** are shown in Figs. 2 and 3, respectively. Table 3 summarizes the calculated values of *Ea* and the corresponding yields of adducts. Cycloaddition of quinolone **1** and dienes **6**—**8** favored the *endo*-adducts, but cycloaddition of **2**—**4** with **5**—**7** favored the *exo*-adducts. The calculated values of *Ea* are consistent with these results.

Cycloaddition of quinolone **1** and diene **5** primarily produced the *exo*-adduct **10a** at lower temperatures and with shorter reaction times, but largely formed the *endo*-adduct **9a** at higher temperatures and/or longer reaction times (Table 1, entries 1—4). To examine these experimental results, we calculated the difference in heat of formation (*HF*) of *exo-* and *endo*-adducts and showed as ΔE in Table 3. The calculated value of *Ea* for the *exo*-addition is smaller than that for the *endo*-addition (Table 3, entry 1), but the optimized energy of the corresponding *endo*-adduct is 1.20 kcal/mol lower than that of the *exo*-adduct. These experimental and theoretical results can be explained if this reaction proceeded under kinematic control with the former conditions, but under thermodynamic control with the latter conditions. In fact, when an *o*-xylene solution of *exo*-adduct **10a** and **5** was heated at 200 °C for 4 d, the reaction mixture contained *endo*-adduct (**9a**, 19%), quinolone (**1**, 18%), and *exo*-adduct (**10a**, 44% recovery). From this result, we confirm that the retro-cycloaddition reaction proceeded. Cycloaddition of **1** with **8** produced the *endo*-adduct (Table 3, entry 4). We can consider that this reaction proceeded under kinematic control, since the value of *Ea* predicts the *endo*-adduct and that of *HF*

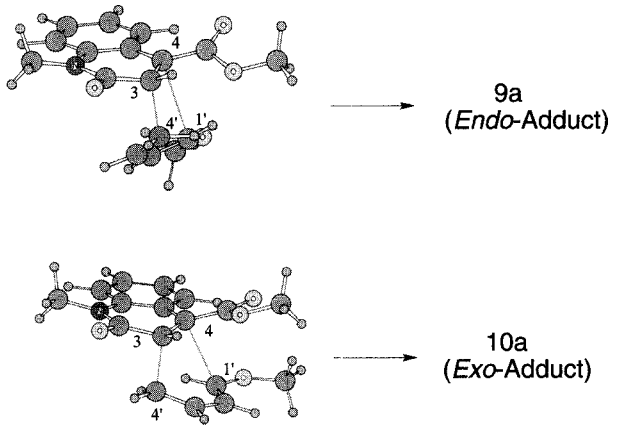

Fig. 2. Calculated Structures of TS for *Endo*-addition (Upper) and for *Exo*-addition (Lower), in Cycloaddition of **1** with **5**, Optimized Using AM1 Method

The calculated relevant interatomic distances are: C_3C_4=1.414 Å, $C_3C_{4'}$=1.807 Å, $C_4C_{1'}$=3.088 Å (upper); and C_3C_4=1.413 Å, $C_3C_{4'}$=1.875 Å, $C_4C_{1'}$=2.688 Å (lower). The corresponding bond orders are: C_3C_4=1.3038, $C_3C_{4'}$=0.5156, $C_4C_{1'}$=0.0853 (upper); and C_3C_4=1.3229, $C_3C_{4'}$=0.4927, $C_4C_{1'}$=0.1261 (lower).

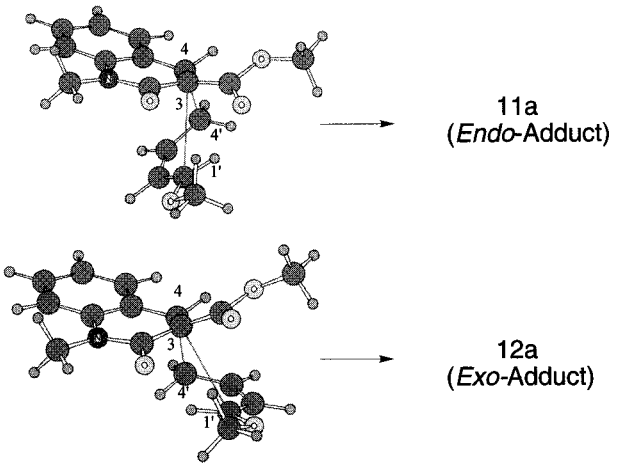

Fig. 3. Calculated Structures of TS for *Endo*-addition (Upper) and for *Exo*-addition (Lower), in Cycloaddition of **3** with **5**, Optimized Using AM1 Method

The calculated relevant interatomic distances are: C_3C_4=1.417 Å, $C_3C_{1'}$=2.940 Å, $C_4C_{4'}$=1.848 Å (upper); and C_3C_4=1.418 Å, $C_3C_{1'}$=2.890 Å, $C_4C_{4'}$=1.861 Å (lower). The corresponding bond orders are: C_3C_4=1.2521, $C_3C_{1'}$=0.0666, $C_4C_{4'}$=0.5087 (upper); and C_3C_4=1.2536, $C_3C_{1'}$=0.0704, $C_4C_{4'}$=0.5059 (lower).

Table 3. Yields of Adducts and Activation Energies for Cycloadditions of **1**—**4** with **5**—**8** Calculated Using AM1 Method

Entry	Quinolone No.	Diene No.	Temp. (°C)	Time (d)	*Endo*-addition			*Exo*-addition			$\Delta Ea^{a)}$ (kcal/mol)	$\Delta E^{b)}$ (kcal/mol)
					Adduct No.	*Ea* (kcal/mol)	Yield (%)	Adduct No.	*Ea* (kcal/mol)	Yield (%)		
1	**1**	**5**	160	4	**9a**	31.76	14	**10a**	31.72	59	−0.04	1.20
2	**1**	**6**	180	6	**9c**	28.93	39	**10c**	29.40	29	0.47	0.84
3	**1**	**7**	180	6	**9e**	33.51	30	**10e**	34.15	0	0.64	2.15
4	**1**	**8**	160	6	**9g**	39.24	38	**10g**	41.40	0	2.16	−2.59
5	**2**	**5**	180	3	**9b**	34.04	27	**10b**	32.59	30	−1.45	−2.24
6	**2**	**6**	160	6	**9d**	32.45	19	**10d**	31.41	41	−1.04	−3.11
7	**2**	**7**	180	6	**9f**	36.91	7	**10f**	35.91	12	−1.00	−1.83
8	**3**	**5**	180	6	**11a**	32.25	3	**12a**	32.17	14	−0.08	−1.25
9	**4**	**5**	180	6	**11b**	33.79	0	**12b**	33.08	25	−0.71	−2.48
10	**4**	**6**	180	6	**11d**	29.67	0	**12d**	28.88	6	−0.79	−3.81

a) Difference in activation energies (*Ea*) between *exo*- and *endo*-addition. *b*) Difference in heat of formation between *exo*- and *endo*-adducts.

expects the *exo*-adduct. For the other reactions in Table 3 (entries 2, 3, 5—10), the calculated values of *Ea* and *HF* both predict the same product.

We also theoretically study the *endo*-/*exo*-selectivity of the cycloaddition reactions under the condition of high pressure (HP). In general, the activation volumes of these cycloadition reactions are negative and the reactions will be accelerated under HP. The difference in volume (ΔVa) between TS leading to *exo*- and *endo*-adduct will influence the *endo*-/*exo*-selectivity. We calculated the volume of TS and obtained ΔVa for four reactions in Table 2 (entries 4, 5, 7, 8) using Gaussian 98 with the 6-31G(d) basis set.[27] For reaction of **2** with **7**, the calculated ΔVa is $-2.86\,cm^3$/mol, which enhances the *exo*-selectivity under HP (Table 2, entry 8). For cycloadition of **1** with **6**, the calculated ΔVa has the magnitude of $-3.16\,cm^3$/mol, which is large enough to compensate the value of *Ea* and to change the primary product from *endo*- to *exo*-adduct under HP (Table 2, entry 5), since $\Delta Va = 1\,cm^3$/mol corresponds to 0.24 kcal/mol under the pressure of 10 kbar. For cycloaddition of **4** with **5** and **1** with **7**, the calculated values of ΔVa are 0.87 and $-0.89\,cm^3$/mol, respectively. These values are too small to alter the *endo*-/*exo*-selectivity of the products (Table 2, entries 4, 7).

In conclusion, we prepared the desired richly functionalized phenanthridines using cycloaddition of 1-substituted 1,3-butadienes with 2(1*H*)-quinolones having an electron-withdrawing group at the 4- or 3-position. We have also developed a methodology for phenanthridine synthesis. Furthermore, with regard to the reactivity of 4- or 3-substituted 2(1*H*)-quinolones using the MO calculation, calculated activation energies were well correlated with experimental yields of the adducts.

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 tetramethylsilane (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 Cycloaddition of 1, 2, 3 and 4 with 5 a) An *o*-xylene solution (3 ml) of **1** (217 mg, 1 mmol) and **5** (860 mg, 5 mmol) was heated at 160 °C for 4 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 ethyl acetate–hexane (1 : 1) was evaporated to give 5,6,6a,7,10,10a-hexahydro-10α-methoxy-*cis*-10a-methoxycarbonyl-5-methyl-6-oxo-phenanthridine (**9a**). The second fraction eluted with ethyl acetate–hexane (1 : 1) was evaporated to give 5,6,6a,7,10,10a-hexahydro-10β-methoxy-*cis*-10a-methoxycarbonyl-5-methyl-6-oxo-phenanthridine (**10a**). b) Reactions of **1**, **2**, **3** and **4** (1 mmol) with **5** (5 mmol) were carried out under the conditions listed in Table 1 and products were purified as described above to give **9a**, **10a**, *cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-10α-methoxy-5-methyl-6-oxo-phenanthridine (**9b**), *cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-10β-methoxy-5-methyl-6-oxo-phenanthridine (**10b**), 5,6,6a,7,10,10a-hexahydro-7α-methoxy-*cis*-6a-methoxycarbonyl-5-methyl-6-oxo-phenanthridine (**11a**), 5,6,6a,7,10,10a-hexahydro-7β-methoxy-*cis*-6a-methoxycarbonyl-5-methyl-6-oxo-phenanthridine (**12a**), and *cis*-6a-cyano-5,6,6a,7,10,10a-hexahydro-7β-methoxy-5-methyl-6-oxo-phenanthridine (**12b**), respectively. The respective yields of the above compounds are summarized in Table 1.

9a: Colorless needles (ether), mp 159—163 °C. IR (KBr) cm^{-1}: 2822, 1723, 1678, 1599, 1135. ^{1}H-NMR ($CDCl_3$) δ: 2.17—2.24 (1H, m, H-7), 2.91—2.97 (1H, m, H-7), 2.98 (3H, s, OMe), 3.34 (3H, s, NMe), 3.44 (1H, ddd, J=2.5, 5.6, 5.6 Hz, H-6a), 3.77 (3H, s, OMe), 4.22 (1H, dd, J=0.7, 4.5 Hz, H-10), 5.81 (1H, ddd, J=2.6, 4.3, 7.8 Hz, H-8), 5.95 (1H, ddd, J=2.3, 4.4, 8.0 Hz, H-9), 7.00—7.06 (2H, m, H-aromatic), 7.22—7.36 (2H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 22.86, 30.21, 38.82, 52.73, 53.05, 58.82, 77.21, 115.29, 122.62, 125.04, 125.26, 126.24, 128.15, 128.56, 141.54, 169.35, 172.92. MS *m*/*z*: 301 (M^+), 217. HR-MS *m*/*z*: Calcd for $C_{17}H_{19}NO_4$, 301.1314. Found: 301.1320.

10a: Colorless needles (ether), mp 147 °C. IR (KBr) cm^{-1}: 2819, 1738, 1683, 1598, 1143. ^{1}H-NMR ($CDCl_3$) δ: 1.57—1.75 (1H, m, H-7), 2.40—2.51 (1H, m, H-7), 3.32 (3H, s, OMe), 3.39—3.47 (4H, br s, NMe, H-6a), 3.65 (3H, s, OMe), 4.50 (1H, d, J=5.1 Hz, H-10), 5.81 (1H, ddd, J=2.6, 4.6, 7.6 Hz, H-8), 6.08 (1H, ddd, J=2.7, 4.8, 7.6 Hz, H-9), 6.95—6.98 (1H, m, H-aromatic), 7.03—7.09 (1H, ddd, J=1.1, 7.8, 7.8 Hz, H-9), 7.21—7.33 (2H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 22.60, 31.54, 37.49, 52.38, 57.26, 60.33, 73.07, 114.67, 122.09, 122.71, 123.15, 126.75, 128.72, 131.02, 140.17, 171.08, 171.79. MS *m*/*z*: 301 (M^+), 217. HR-MS *m*/*z*: Calcd for $C_{17}H_{19}NO_4$, 301.1314. Found: 301.1338.

9b: Pale yellow needles (acetone), mp 139—141 °C. IR (KBr) cm^{-1}: 2820, 2242, 1676, 1600, 1135. ^{1}H-NMR ($CDCl_3$) δ: 2.43—2.54 (1H, m, H-7), 2.84 (3H, s, NMe), 3.10 (1H, dd, J=5.7, 7.1 Hz, H-6a), 3.17 (1H, dddd, J=4.0, 5.7, 5.7, 18.5 Hz, H-7), 3.27 (3H, s, OMe), 3.76 (1H, d, J=4.6 Hz, H-10), 5.84 (1H, ddd, J=2.5, 4.6, 10.4 Hz, H-9), 6.00 (1H, ddd, J=2.5, 5.0, 10.4 Hz, H-8), 6.98 (1H, dd, J=1.0, 8.2 Hz, H-4), 7.10 (1H, ddd, J=1.0, 7.6, 7.9 Hz, H-2), 7.34 (1H, ddd, J=1.5, 7.9, 8.2 Hz, H-3), 7.61 (1H, dd, J=1.5, 7.9 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 21.63, 29.47, 37.53, 42.97, 58.43, 114.74, 119.03, 120.87, 121.72, 122.32, 126.11, 128.85, 128.91, 130.58, 140.18, 165.92. MS *m*/*z*: 268 (M^+), 184. HR-MS *m*/*z*: Calcd for $C_{16}H_{16}N_2O_2$, 268.1212. Found: 268.1215.

10b: Pale yellow needles (acetone), mp 136—139 °C. IR (KBr) cm^{-1}: 2831, 2242, 1677, 1600, 1135. ^{1}H-NMR ($CDCl_3$) δ: 2.64 (1H, dddd, J=2.8, 5.9, 5.9, 18.8 Hz, H-7), 3.10 (1H, ddd, J=2.0, 4.7, 18.8 Hz, H-7), 3.19 (4H, br s, NMe, H-6a), 3.41 (3H, s, OMe), 3.78 (1H, dd, J=2.0, 3.3 Hz, H-10), 5.81 (1H, ddd, J=2.0, 4.5, 10.9 Hz, H-9), 5.96 (1H, ddd, J=2.4, 2.8, 10.9 Hz, H-10), 7.08 (1H, dd, J=1.1, 8.0 Hz, H-4), 7.21 (1H, ddd, J=1.1, 7.6, 8,0 Hz, H-2), 7.43 (1H, ddd, J=1.5, 7.6, 8.0 Hz, H-3), 7.71 (1H, dd,

J=1.5, 7.6 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 22.88, 30.40, 42.12, 45.24, 45.24, 58.69, 115.41, 118.68, 122.82, 123.28, 123.66, 124.56, 128.50, 129.83, 138.06, 166.87. MS *m/z*: 268 (M^+), 184, 154. HR-MS *m/z*: Calcd for $C_{16}H_{16}N_2O_2$, 268.1212. Found: 268.1230.

11a: Colorless needles (ether), mp 148—151 °C. IR (KBr) cm^{-1}: 2820, 1737, 1665, 1600, 1139. ^{1}H-NMR ($CDCl_3$) δ: 2.33—2.34 (2H, m, H-10, 10), 3.31 (3H, s, OMe), 3.40 (3H, s, NMe), 3.61 (4H, br s, OMe, H-10a), 4.39 (1H, ddd, J=2.4, 2.4, 4.8 Hz, H-7), 5.70 (1H, ddd, J=3.5, 5.6, 7.2 Hz, H-8), 5.98 (1H, ddd, J=2.3, 4.9, 7.2 Hz, H-9), 6.95—7.04 (2H, m, H-aromatic), 7.13 (1H, dd, J=1.5, 7.4 Hz, H-aromatic), 7.25 (1H, ddd, J=1.5, 7.4, 7.8 Hz, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 29.83, 52.88, 57.87, 58.87 (C2), 77.22, 114.45, 123.07 (C2), 124.62, 126.00, 126.85, 127.09, 127.90, 139.96, 166.84, 171.51. MS *m/z*: 301 (M^+), 242, 210. HR-MS *m/z*: Calcd for $C_{17}H_{19}NO_4$, 301.1314. Found: 301.1315.

12a: Colorless needles (ether), mp 123—127 °C. IR (KBr) cm^{-1}: 2827, 1746, 1667, 1603, 1124. ^{1}H-NMR ($CDCl_3$) δ: 1.87—2.00 (1H, m, H-10), 2.39—2.49 (1H, m, H-10), 3.37 (3H, s, OMe), 3.42 (3H, s, NMe), 3.58 (4H, br s, OMe, H-10a), 4.68 (1H, dd, J=1.3, 4.8 Hz, H-7), 5.89 (1H, ddd, J=2.3, 4.8, 8.1 Hz, H-8), 6.14 (1H, ddd, J=2.3, 4.6, 8.1 Hz, H-9), 6.96 (1H, d, J=8.1 Hz, H-aromatic), 7.03—7.09 (1H, ddd, J=1.0, 7.5, 7.5 Hz, H-aromatic), 7.21—7.29 (2H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 29.74, 30.40, 33.20, 52.43, 56.98, 57.51, 115.39, 123.84, 124.26, 127.48, 127.72, 127.75, 128.87, 130.79, 137.51, 165.01, 168.38. MS *m/z*: 301 (M^+), 242, 218. HR-MS *m/z*: Calcd for $C_{17}H_{19}NO_4$, 301.1314. Found: 301.1315.

12b: Coloreless needles (ether), mp 160—162 °C. IR (KBr) cm^{-1}: 1720, 2820, 2236, 1683, 1605, 1130. ^{1}H-NMR ($CDCl_3$) δ: 2.00 (1H, dd, J=10.7, 19.1 Hz, H-10), 2.42—2.54 (1H, m, H-10), 3.43 (3H, s, NMe), 3.50 (1H, dd, J=6.6, 10.5 Hz, H-10a), 3.60 (3H, s, OMe), 4.48 (1H, d, J=4.7 Hz, H-7), 5.86 (1H, ddd, J=2.5, 4.7, 10.2 Hz, H-8), 6.03—6.11 (1H, m, H-9), 7.08—7.17 (2H, m, H-aromatic), 7.26 (1H, dd, J=2.5, 8.3 Hz, H-aromatic), 7.36 (1H, ddd, J=1.5, 7.6, 7.6 Hz, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 28.75, 30.74, 35.32, 47.20, 58.64, 72.33, 115.92, 117.29, 123.98, 124.39, 127.46, 127.70, 128.04, 128.83, 138.11, 161.80. MS *m/z*: 268 (M^+), 185. HR-MS *m/z*: Calcd for $C_{16}H_{16}N_2O_2$, 268.1212. Found: 268.1231.

Typical Procedure for Cycloaddition of 1, 2 and 4 with 6 a) An *o*-xylene solution (3 ml) of **1** (217 mg, 1 mmol) and **6** (710 mg, 5 mmol) was heated at 160 °C for 6 d in a sealed tube. The reaction mixture was concentrated *in vacuo* and diluted with chloroform. To the reaction mixture, TFA (1 ml) was added with stirring at room temperature for 20 min and concentrated *in vacuo.* The residue was subjected to chromatography on a silica gel column. The first fraction eluted with ethyl acetate–hexane (1 : 1) was evaporated to give 5,6,6a,7,10,10a-hexahydro-10α-hydroxy-*cis*-10a-methoxycarbonyl-5-methyl-6-oxo-phenanthridine (**9c**). The second fraction eluted with ethyl acetate–hexane (1 : 1) was evaporated to give 5,6,6a,7,10,10a-hexahydro-10β-hydroxy-*cis*-10a-methoxycarbonyl-5-methyl-6-oxo-phenanthridine (**10c**). b) Reactions of **1**, **2**, **3** and **4** (1 mmol) with **6** (5 mmol) were carried out under the conditions listed in Table 1 and products were purified as described above to give **9c**, **10c**, *cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-10α-hydroxy-5-methyl-6-oxo-phenanthridine (**9d**), *cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-10β-hydroxy-5-methyl-6-oxo-phenanthridine (**10d**), and *cis*-6a-cyano-5,6,6a,7,10,10a-hexahydro-7β-hydroxy-5-methyl-6-oxo-phenanthridine (**12d**), respectively. The respective yields of the above compounds are summarized in Table 1.

9c: Colorless needles (ether), mp 113—116 °C. IR (KBr) cm^{-1}: 3435, 3416, 1720, 1645, 1600. ^{1}H-NMR ($CDCl_3$) δ: 2.21 (1H, dddd, J=1.8, 3.8, 3.8, 16.7 Hz, H-7), 2.97—3.08 (1H, m, H-7), 3.34 (3H, s, NMe), 3.45 (1H, dd, J=2.7, 6.8 Hz, H-6a), 3.78 (3H, s, OMe), 4.46 (1H, br d, J=4.4 Hz, H-10), 5.86 (1H, ddd, J=2.0, 2.0, 8.1 Hz, H-9), 5.93 (1H, ddd, J=2.0, 2.0, 8.1 Hz, H-8), 7.02—7.09 (2H, m, H-3, 4), 7.25 (1H, dd, J=1.5, 7.3 Hz, H-1), 7.34 (1H, ddd, J=1.5, 7.3, 7.3 Hz, H-2). ^{13}C-NMR ($CDCl_3$) δ: 22.78, 30.19, 38.08, 52.83, 3.21, 67.77, 115.45, 123.13, 124.83, 126.29, 126.59, 128.75, 128.92, 141.41, 169.64, 172.80. MS *m/z*: 287 (M^+), 218, 158. HR-MS *m/z*: Calcd for $C_{16}H_{17}NO_4$, 287.1158. Found: 287.1131.

10c: Colorless needles (ether), mp 236—239 °C. IR (KBr) cm^{-1}: 3315, 1728, 1650, 1596. ^{1}H-NMR ($CDCl_3$) δ: 2.18 (1H, m, H-7), 2.65 (1H, d, J=18.8 Hz, H-7), 3.38 (3H, s, NMe), 3.43 (1H, dd, J=4.1, 9.9 Hz, H-6a), 3.78 (3H, s, OMe), 4.47 (1H, br s, H-10), 5.72—5.79 (1H, m, H-9), 5.84—5.89 (1H, m, H-8), 7.02—7.12 (3H, m, H-2, 3, 4), 7.31—7.35 (1H, m, H-1). ^{13}C-NMR ($CDCl_3$) δ: 23.54, 30.11, 40.52, 52.43, 52.81, 67.24, 115.38, 123.28, 124.39, 126.99, 127.59, 128.89, 129.22, 139.27, 169.45, 173.70. MS *m/z*: 287 (M^+), 218. HR-MS *m/z*: Calcd for $C_{16}H_{17}NO_4$, 287.1158. Found: 287.1132.

9d: Colorless needles (ether), mp 172—174 °C. IR (KBr) cm^{-1}: 3416, 2243, 1680, 1597. ^{1}H-NMR ($CDCl_3$) δ: 2.64 (1H, ddd, J=5.6, 6.0, 18.4 Hz, H-7), 3.15 (1H, dddd, J=1.8, 3.8, 4.8, 18.4 Hz, H-7), 3.23 (1H, dd, J=3.8, 5.6 Hz, H-6a), 3.89 (3H, s, NMe), 4.26 (1H, dd, J=2.0, 4.3 Hz, H-10), 5.66—5.72 (1H, m, H-9), 5.94—6.02 (1H, m, H-8), 7.08 (1H, dd, J=1.0, 8.1 Hz, H-4), 7.21 (1H, ddd, J=1.0, 7.6, 7.6 Hz, H-2), 7.44 (1H, ddd, J=1.0, 7.6, 8.1 Hz, H-3), 7.68 (1H, dd, J=1.5, 7.6 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 22.82, 30.40, 41.67, 46.98, 68.00, 115.68, 118.36, 122.20, 123.76, 127.07, 128.01, 128.89, 130.05, 138.14, 166.64. MS *m/z*: 254 (M^+), 185. HR-MS *m/z*: Calcd for $C_{15}H_{14}N_2O_2$, 254.1055. Found: 254.1064.

10d: Colorless needles (ether), mp 156—158 °C. IR (KBr) cm^{-1}: 3442, 2244, 1682, 1601. ^{1}H-NMR ($CDCl_3$) δ: 2.54 (1H, dddd, J=2.5, 4.1, 6.8, 18.6 Hz, H-7), 3.13 (1H, d, J=6.8 Hz, H-6a), 3.19—3.35 (4H, m, NMe, H-7), 4.23 (1H, br s, H-10), 5.83—5.90 (1H, m, H-9), 6.03—6.10 (1H, m, H-8), 7.03 (1H, dd, J=1.1, 8.1 Hz, H-4), 7.16 (1H, ddd, J=1.1, 7.8, 8.1 Hz, H-2), 7.40 (1H, ddd, J=1.5, 8.1, 8.1 Hz, H-3), 7.68 (1H, dd, J=1.5, 7.8 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 22.49, 30.33, 37.79, 44.53, 68.58, 115.71, 119.92, 121.48, 123.60, 124.16, 127.19, 130.00, 130.24, 140.95, 167.00. MS *m/z*: 254 (M^+), 185. HR-MS *m/z*: Calcd for $C_{15}H_{14}N_2O_2$, 254.1055. Found: 254.1085.

12d: Coloreless needles (acetone–hexane), mp 184—186 °C. IR (KBr) cm^{-1}: 3371, 2243, 1672, 1605, 758. ^{1}H-NMR (CD_3OD) δ: 2.00—2.18 (1H, m, H-10), 2.50 (1H, ddd, J=2.6, 6.2, 20.3 Hz, H-10), 3.42 (3H, s, NMe), 3.54 (1H, dd, J=6.0, 9.0 Hz, H-10a), 4.67 (1H, br s, H-7), 5.79—5.88 (2H, m, H-8,9), 7.16 (1H, ddd, J=1.1, 7.3, 7.3 Hz, H-aromatic), 7.29 (1H, d, J=8.3 Hz, H-aromatic), 7.34—7.43 (2H, m, H-aromatic). ^{13}C-NMR (CD_3OD) δ: 28.74, 31.0, 36.47, 48.61, 49.47, 117.23, 118.70, 125.46, 127.82, 128.13, 128.44, 128.64, 129.93, 139.80, 164.09. MS *m/z*: 254 (M^+), 185. HR-MS *m/z*: Calcd for $C_{15}H_{14}N_2O_2$, 254.1055. Found: 254.1078.

Typical Procedure for Cycloaddition of 1 and 2 with 7 a) An *o*-xylene solution (3 ml) of **1** (217 mg, 1 mmol) and **7** (560 mg, 5 mmol) was heated at 160 °C for 6 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–hexane (1 : 1) was evaporated to give 10α-acetoxy-5,6,6a,7,10,10a-hexahydro-*cis*-10a-methoxycarbonyl-5-methyl-6-oxo-phenanthridine (**9e**). b) A *o*-xylene solution (3 ml) of **2** (0.092 g, 0.5 mmol) and **7** (0.28 mmol, 2.5 mmol) was heated at 160 °C for 6 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 ethyl acetate–hexane (3 : 1) was evaporated to give 10α-acetoxy-*cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-5-methyl-6-oxo-phenanthridine (**9f**). The second fraction eluted with ethyl acetate–hexane (3 : 1) was evaporated to give 10β-acetoxy-*cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-5-methyl-6-oxo-phenanthridine (**10f**). The respective yields of the above compounds are summarized in Table 1.

9e: Colorless oil. IR (KBr) cm^{-1}: 1736, 1674, 160. ^{1}H-NMR ($CDCl_3$) δ: 1.61 (3H, s, COMe), 2.19—2.27 (1H, m, H-7), 3.20 (1H, dd, J=4.5, 18.7 Hz, H-7), 3.40 (3H, s, NMe), 3.52 (1H, d, J=6.8 Hz, H-6a), 3.83 (3H, s, OMe), 5.79—5.86 (1H, m, H-9), 5.93 (1H, d, J=5.1 Hz, H-10), 5.98—6.04 (1H, m, H-8), 7.00—7.12 (3H, m, H-2, 3, 4), 7.30—7.36 (1H, m, H-1). ^{13}C-NMR ($CDCl_3$) δ: 20.41, 22.19, 30.30, 38.08, 52.14, 53.08, 67.95, 115.03, 123.14, 123.21, 124.19, 126.55, 129.13, 130.64, 140.93, 168.84, 169.12, 171.94. MS *m/z*: 329 (M^+), 217, 210. HR-MS *m/z*: Calcd for $C_{18}H_{19}NO_5$, 329.1263. Found: 329.1234.

9f: Colorless needles (hexane–acetone), mp 159—160 °C. IR (KBr) cm^{-1}: 2248, 1742, 1681, 1604, 765. ^{1}H-NMR ($CDCl_3$) δ: 2.02—2.18 (4H, s, COMe, H-7), 2.68 (1H, dddd, J=2.9, 5.9, 5.9, 18.8 Hz, H-7), 3.16—3.22 (1H, br m, H-6a), 3.42 (3H, s, NMe), 5.47 (1H, d, J=1.8 Hz, H-10), 5.61 (1H, ddd, J=1.8, 4.3, 10.6 Hz, H-9), 6.01 (1H, ddd, J=2.3, 4.8, 10.6 Hz, H-8), 7.07 (1H, dd, J=0.8, 7.7 Hz, H-4), 7.16 (1H, ddd, J=0.8, 7.6, 7.6 Hz, H-2), 7.43 (1H, ddd, J=1.6, 7.6, 7.7 Hz, H-3), 7.58 (1H, dd, J=1.5, 7.6 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 20.65, 22.83, 30.54, 41.98, 44.09, 68.71, 115.83, 118.08, 121.40, 123.63, 124.12, 127.31, 129.57, 130.34, 138.38, 166.26, 169.75. MS *m/z*: 296 (M^+), 227, 185. HR-MS *m/z*: Calcd for $C_{17}H_{16}N_2O_3$, 296.1161. Found: 296.1125.

10f: Pale yellow needles (ether), mp 95—97 °C. IR (KBr) cm^{-1}: 2242, 1730, 1677, 1600, 773. ^{1}H-NMR ($CDCl_3$) δ: 2.04 (3H, s, COMe), 2.55—2.70 (1H, m, H-7), 3.20 (1H, d, J=6.7 Hz, H-6a), 3.24—3.41 (1H, m, H-7), 3.39 (3H, s, NMe), 5.54 (1H, d, J=4.6 Hz, H-10), 5.79 (1H, ddd, J=2.8, 4.6, 10.6 Hz, H-9), 6.22 (1H, ddd, J=2.5, 5.3, 10.6 Hz, H-8), 7.03 (1H, dd, J=1.0, 8.2 Hz, H-4), 7.18 (1H, ddd, J=1.0, 7.6, 8.2 Hz, H-2), 7.43 (1H, ddd, J=1.5, 8.2, 8.2 Hz, H-3), 7.65 (1H, dd, J=1.5, 7.6 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 20.14, 22.39, 30.46, 38.56, 43.14, 67.66, 115.23, 119.23, 120.56, 121.11, 123.79, 128.08, 130.37, 131.95, 140.40, 166.31, 168.52. MS *m/z*: 296 (M^+), 227, 185. HR-MS *m/z*: Calcd for $C_{17}H_{16}N_2O_3$, 296.1161. Found: 296.1200.

Cycloaddition of 1 with 8 a) An *o*-xylene solution (3 ml) of **1** (217 mg, 1 mmol) and **8** (510 mg, 3 mmol) was heated at 160 or 180 °C for 6 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 acetone–hexane (1 : 2) was evaporated. The crude product was purified by preparative TLC on silica gel with diisopropyl ether–acetone (3 : 1) to give 7α,10α-diacetoxy-5,6,6a,7,10,10a-hexahydro-*cis*-10a-methoxy-carbonyl-5-methyl-6-oxo-phenanthridine (**9g**). Yields of **9g** are summarized in Table 1.

9g: Colorless needles (ether), mp 135—138 °C. IR (KBr) cm^{-1}: 1745, 1720, 1681, 1604. ^{1}H-NMR ($CDCl_3$) δ: 1.83 (3H, s, COMe), 1.90 (3H, s, COMe), 3.37 (3H, s, NMe), 3.77 (3H, s, OMe), 3.82 (1H, d, J=5.8 Hz, H-6a), 5.45 (1H, ddd, J=2.0, 4.5, 5.8 Hz, H-7), 5.82 (1H, ddd, m, H-8 or 9), 5.95 (1H, ddd, m, H-8 or 9), 6.05 (1H, ddd, J=1.5, 3.4, 4.9 Hz, H-10), 6.71—7.09 (2H, m, H-aromatic), 7.30—7.38 (2H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 14.16, 20.52, 20.83, 29.95, 53.40, 60.34, 114.76, 115.52, 116.08, 123.10, 123.50, 123.64, 127.40, 128.93, 129.68, 141.71, 169.19, 170.00, 171.09, 171.80. MS *m*/*z*: Calcd for $C_{20}H_{21}NO_7$, 387.1318. Found: 387.1302.

Typical Procedure for Cycloaddition of 1, 2, 3 and 4 with 5, 6, 7 and 8 under HP Conditions a) A mixture of **1** (43 mg, 0.2 mmol) and **5** (84 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 **9a**, and **10a**. b) Reaction of **1** (0.2 mmol) with **6** (1 mmol) in dichloromethane (3 ml) was placed in a Teflon tube, and subjected to the reaction condition listed in Table 2. The reaction mixture was treated with TFA, and concentrated *in vacuo*. Residues were treated as described above to give **9c** and **10c**. c) Reactions of **2**—**4** (0.2 mmol) with **5** (1 mmol), **2** (0.2 mmol) with **6** (1 mmol), **1**, **2** (0.2 mmol) with **7** (1 mmol) and **1** (0.2 mmol) with **8** (1 mmol) in dichloromethane (3 ml) were placed in a Teflon tube, and subjected to the reaction conditions listed in Table 2. The reaction mixtures were treated as described above to give **9a**—**g**, **10a**—**f**, **11a** and **12a** and **b**. Yields are summarized in Table 2.

Retro-cycloaddition of 10a An *o*-xylene solution (3 ml) of **10a** (16 mg, 0.05 mmol) and **5** (21 mg, 0.25 mmol) was heated at 200 °C for 4 d in a sealed tube. The reaction mixture was concentrated *in vacuo*, and the crude product was purified by preparative TLC on silica gel with hexane–ethyl acetate (1 : 1) to give **9a** (3 mg, 19%), **1** (2 mg, 18%) and the recovery of **10a** (7 mg, 44%).

Calculation of Activation Energy and Volume Structures of the initial and the transition states (TS) were optimized using the semi-empirical molecular orbital AM1 method in the MOPAC 2000 software package.[26] The effect of the solvent was not considered. We assumed that the diene and the dienophile were in equilibrium attracting each other by van der Waals interactions in the initial state. We calculated the activation energy as the difference in energy between the TS and initial state. After optimizing the TS structure, vibrational calculation was performed to confirm that the TS had only one imaginary vibrational frequency. Intrinsic reaction coordinate calculation was also carried out to ensure that the TS connected the initial and intended final states.

We calculated volumes of TS, using the structures obtained above, inside a contour of 0.001 electrons/bohr^3 (1 bohr=0.529Å), using Gaussian 98 with the 6-31G (d) basis set and Volume=Tight option.[27] We carried out about 20 times of run to improve the precision of volume calculation, since a Monte-Carlo integration is done in the routine.

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