Diels–Alder Reaction of 1,3-Butadiene Derivatives with 1-Methyl-2(1*H*)-quinolones Having an Electron-Withdrawing Group at the 4-Position

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Diels–Alder reactions of 1-methyl-2(1*H*)-quinolones having an electron-withdrawing group at the 4-position with isoprene, butadiene sulfone, and cyclohexadiene were performed to yield functionalized phenanthridones stereoselectively at atmospheric and at high pressure. Regioselectivity and stereochemistry of a methoxycarbonyl group were studied using the semi-empirical and *ab initio* MO methods, respectively.

Key words 1-methyl-2(1*H*)-quinolone; phenanthridone; isoprene; butadiene sulfone; electron-withdrawing group; MO calculation

2(1*H*)-Quinolones are aromatic and many substitution reactions have been reported.[1] Nakagawa and co-workers. reported the first example, a Diels–Alder (DA) reaction of 1-methoxy- carbonyl-3-phenylthio-2(1*H*)-quinolone with 2-silyloxy-1,3-butadiene to give the intermediate (phenanthridone derivative) for a marine alkaloid (Dynemisine A).[2] In addition, an aromatized or hydrogenated phenanthridone skeleton is a feature of many Amarylidaceae alkaloids.[3] Therefore, richly functionalized phenanthridones shoud be valuable synthetic intermediates. We recently reported the synthesis of phenanthridones richly functionalized using the DA reaction of 2(1*H*)-quinolones having an electron-withdrawing group at the 4-position with Danishefsky's diene, as well as 2-trimethylsilyloxy-, dimethyl-, and dimethoxy-1,3-butadienes.[4] DA reactions of cyclic 1,3-butadiene and the unsynmetric alkyldiene with 2(1*H*)-quinolones have not yet been described. A phenanthridone in which the ene part at the 8,9- positions lack substituent groups would be useful. Here, we describe the synthesis of phenanthridones by the uncatalyzed and thermal DA reaction of 1-methyl-2(1*H*)-quinolones having an electron-withdrawing group at the 4-position with isoprene, butadiene sulfone, and cyclohexadiene at atmospheric and high pressure (AP and HP[5]). Furthermore, we investigated the regioselectivety of isoprene and stabilization energies for the reaction of cyclohexadiene with 2(1*H*)-quinolones using the MO calculation .

DA Reaction Firstly, DA reactions of 1-methyl-2(1*H*)-quinolones having an electron-withdrawing group [such as methoxycarbonyl- (**1a**),[6] cyano- (**1b**),[7] acetyl- (**1c**),[4] and benzoyl- (**1d**),[8]] at the 4-position with a unsymmetric diene (**2a**) were examined under AP shown in Table 1 and Chart 1. The reactions of **1a**—**d** with isoprene (**2a**) stereoselectively yielded the main adducts [5,8-dimethylphenanthridones (**3a**—**d**), entries 1, 3, 5, 7] and the minor adducts [5,9-dimethylphenanthridones (**3e**, **f**), entries 3, 5] at 180 °C. The formation of the 9-methylphenanthridone (**3g**) in the DA reaction of **1d** with **2a** was identified by ^{1}H-NMR spectral analysis, but **3g** was not separated from the reaction mixture. Also, DA reactions of **1a**—**d** with **2a** were attempted under HP as shown in Table 1. However, these reactions did not yield the satisfactory results.

Furthermore, DA reactions of **1a**—**c** with **2b** at AP stereoselectively afforded **4a**—**c** in 29—37% yields (Table 1 and Chart 1). However, reaction of **1d** with **2b** did not give **4d** and **1d** was recovered. Reaction of **1a** with cyclic diene (**2c**) at AP yielded *cis*-[**5a** (15%)] and *trans*-adducts [**5b** (6%)]. The same reaction under HP gave only the *cis*-adduct [**5a** (18%)]. Also, isomerization of **5a** with lithium diisopropylamide (LDA) at −78 °C gave **5b** (5%) with recovery of the starting material.

We confirmed the stereochemistry of the ring juncture in **3a**—**f**, **4a**—**c**, and **5a**, **b** as follows. We confirmed that in the DA reactions of 2(1*H*)-quinolones with 2,3-dimethyl-1,3-butadiene, the stereochemistries of the ring juncture in the 6(5*H*)-phenanthridone derivatives (A) are *cis*- or *trans*-form, by X-ray crystallography and by measuring the nuclear Overhauser effect (NOE) of ^{1}H-NMR spectra (Fig. 1).[4] The signals (δ 3.04—3.41) due to H-6a in the *cis*-A appeared at a

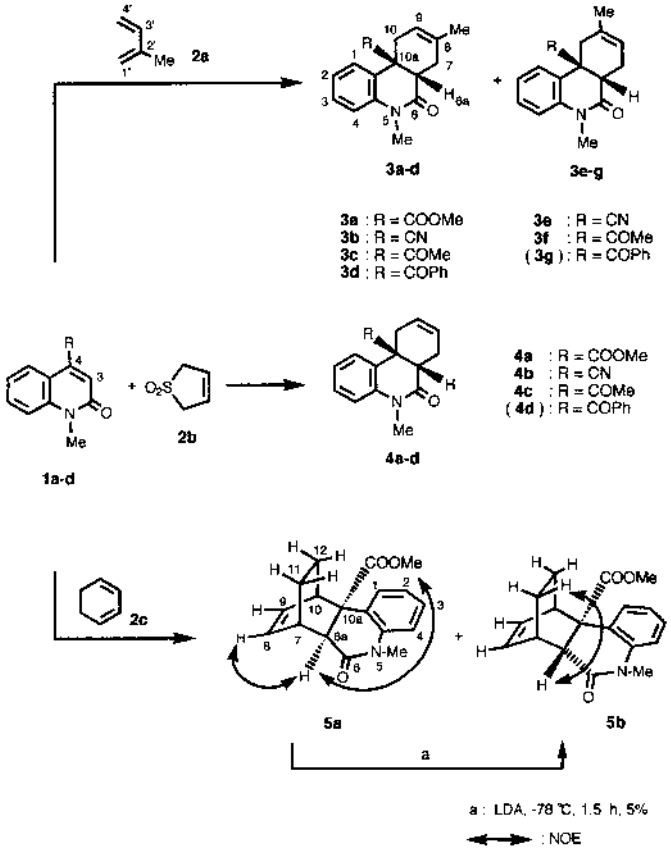

Chart 1

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Table 1. DA Reactions of **1a**—**d** with **2a**—**c**

Entry	Substrate	Diene	Temp. (°C)	Time (d)	Solvent	Pressure (kbar)	Adduct	Yield (%)	Adduct	Yield (%)
1	**1a**	**2a**	180	5	*o*-Xylene	Atmospheric	**3a**	42		
2	**1a**	**2a**	80	2	CH_2Cl_2	5	**3a**	14		
3	**1b**	**2a**	180	5	*o*-Xylene	Atmospheric	**3b**	43[a]	**3e**	16[a]
4	**1b**	**2a**	80	2	CH_2Cl_2	5	**3b**	10	**3e**	—
5	**1c**	**2a**	180	5	*o*-Xylene	Atmospheric	**3c**	42[a]	**3f**	21[a]
6	**1c**	**2a**	80	3	CH_2Cl_2	10	**3c**	5	**3f**	—
7	**1d**	**2a**	180	5	*o*-Xylene	Atmospheric	**3d**	12	(**3g**)[b]	—
8	**1d**	**2a**	90	3	CH_2Cl_2	10	**3d**	—	(**3g**)	—
9	**1a**	**2b**	180	3	*o*-Xylene	Atmospheric	**4a**	29		
10	**1b**	**2b**	180	3	*o*-Xylene	Atmospheric	**4b**	37		
11	**1c**	**2b**	180	3	*o*-Xylene	Atmospheric	**4c**	33		
12	**1d**	**2b**	180	3	*o*-Xylene	Atmospheric	**4d**	—		
13	**1a**	**2c**	180	5	*o*-Xylene	Atmospheric	**5a**	15	**5b**	6
14	**1a**	**2c**	90	3	CH_2Cl_2	10	**5a**	18	**5b**	—

a) Yields obtained by ^{1}H-NMR spectral analysis. *b*) **3g** was identified by ^{1}H-NMR spectral analysis, but, **3g** was not separated from a mixture.

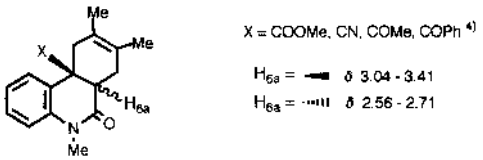

Fig. 1. Chemical Shifts (δ) of A

lower magnetic field than those (δ 2.56—2.71) in the corresponding *trans*-A in the ^{1}H-NMR spectra (Fig. 1).[4] The signals due to H-6a in **3a**—**f** and **4a**—**c** appeared at δ 3.06—3.47 in the ^{1}H-NMR spectra. Furthermore, when H-6a was irradiated in **3a**, **c**, **f** and **4a**, **c**, NOE was observed between H-6a and the corresponding methoxycarbonyl or acetyl group at the 10a-position (Chart 1). Also, when H-6a was irradiated in **5a**, **b**, whereas NOE in **5a** was observed between H-6a and the methoxycarbonyl group at the 10a-position (Chart 1), it was not observed in **5b**. These results confirmed that the stereochemistry of the ring juncture in **3a**—**f**, **4a**—**c** and **5a** was *cis* and that in **5b** was *trans*. The positions on methyl groups in the main (**3a**—**d**) and minor adducts (**3e**, **f**) were assigned by measuring the corresponding ^{1}H-NMR spectra and ^{1}H–^{1}H correlation spectroscopy (COSY). ^{1}H–^{1}H COSY of **3a**—**d** suggested that a methyl group occupied the 8-position, since the olefinic proton and two H-10 correlated. Similarly, the ^{1}H–^{1}H COSY spectra of **3e**, **f** indicated that a methyl group occupied the 9-position, since the olefinic proton and two H-7 correlated. The stereochemistry on the methoxycarbonyl groups in **5a**, **b** was determined by NOE measurements of ^{1}H-NMR spectra on **5a**, **b** (Chart 1). When H-6a in **5a** was irradiated, NOE was observed between H-6a and H-8, but when H-6a in **5b** was irradiated, NOE was not observed between H-6a and the H-8 or a methoxycarbonyl group, but was observed between H-6a and the H-11 (Chart 1). Consequently, the stereochemistry of the methoxycarbonyl groups in **5a**, **b** was *endo*.

Regioselectivity and Stereochemistry Since the diene and the dienophiles are unsymmetrical in the DA reactions of **1a**—**d** with **2a** and **2d** (Danishefsky's diene), regioisomers would be produced. We studied this regioselectivity theoretically using the stabilization energy as a reaction index. We optimized **1a**—**d**, **2a** and **2d** using the semi-empirical molecular orbital AM1 method.[9] Then calculated stabilization energy (ΔE) using the following formula:

$$\Delta E = 2\left(\sum_{D}^{vac}\sum_{P}^{occ} - \sum_{D}^{occ}\sum_{P}^{vac}\right)\frac{(C_r^D C_t^P \gamma_{rt} + C_s^D C_u^P \gamma_{su})^2}{E^D - E^P} \quad (1)$$

Here, D and P indicate the energy levels, E^D and E^P denote the energy eigenvalues of the diene and the dienophile, respectively ; C_r^D and C_t^P are the amplitudes of atoms r and t of the diene and the dienophile, respectively; γ_{rt} and γ_{su} are integrals denoting the amplitudes of interaction between atoms (r–t and s–u, respectively) generating a new bond. We assumed that they have equal values and described them simply as γ. We considered only HOMO and LUMO levels into account in calculating Eq. 1. Table 2 summarizes the calculated values of ΔE together with the experimentally obtained products. Since the values of ΔE for the (1′-3,4′-4)-addition are greater than those for the (1′-4,4′-3)-addition in the DA reactions of **1a**—**d** with **2a** and **2d**, the (1′-3,4′-4)-addition will afford the main products. (The numbers of atoms are shown in Chart 1). The experimental data are consistent with these calculated results (see Tables 1, 2). In the DA reactions of **1a**—**d** with **2d**, the differences in ΔE between the (1′-3, 4′-4)-addition and (1′-4,4′-3)-addition are comparatively large and the products corresponding to the latter were not experimentally obtained. Conversely, in the DA reactions of **1b**—**d** with **2a**, the differences in ΔE are small and the products [**3e**, **f**, (**g**)] corresponding to the latter were experimentally produced in somewhat small yields.

We examined theoretically the stereochemistry of a methoxycarbonyl group in the DA reaction of **1a** with **2c**. We searched and optimized the structures of transition states (TS) of these reactions using Gaussian 98 at the RHF/6-31G (*d*) level.[10] The calculated structures of the TS and the corresponding products are shown in Fig. 2. We assumed that the diene and dienophile were far apart in the initial state. We regarded the difference in energy between TS and the initial state as activation energy (*Ea*). Table 3 summarizes the calculated activation energies of these reactions together with the experimental adducts and their yields. The value of *Ea* for producing **5a** is smaller than that for making **5c**. This result is consistent with the fact that **5a** and **5b** were produced

Table 2. Regioselectivity in DA Reactions of **1a**—**d** with **2a** and **2d** Based on Stabilization Energies (ΔE) Calculated Using AM1

Quinolone	Diene	(1′-3, 4′-4)-Addition[a]		(1′-4, 4′-3)-Addition[a]		Difference[b]
		$\Delta E/\gamma^2$	Adduct	$\Delta E/\gamma^2$	Adduct	
1a	**2a**	0.0998	**3a**	0.0983	—	0.0015
1b	**2a**	0.1036	**3b**	0.1023	**3e**	0.0013
1c	**2a**	0.0943	**3c**	0.0936	**3f**	0.0007
1d	**2a**	0.0869	**3d**	0.0862	(**3g**)	0.0007
1a	**2d**	0.0872	**6a**[c]	0.0821	—	0.0051
1b	**2d**	0.0902	**6b**[c]	0.0855	—	0.0047
1c	**2d**	0.0807	**6c**[c]	0.0785	—	0.0022
1d	**2d**	0.0746	**6d**[c]	0.0719	—	0.0027

a) The numbers of atoms are indicated in Chart 1. *b*) Difference in ΔE between (1′-3,4′-4)-addition and (1′-4,4′-3)-addition. *c*) Adducts (**6a**—**d**) are 6,8-dioxophenanthridine.[4]

Table 3 Stereochemistry of Methoxycarbonyl Group in the DA Reaction of **1a** with **2c** in Terms of Energy (*Ea*) Calculated at RHF/6-31G (d) Level

Quinolone	Diene	*Ea* (kcal/mol)	Adduct	Yield (%)
1a	**2c**	49.98	**5a, 5b**	21
1a	**2c**	50.85	**5c**	—

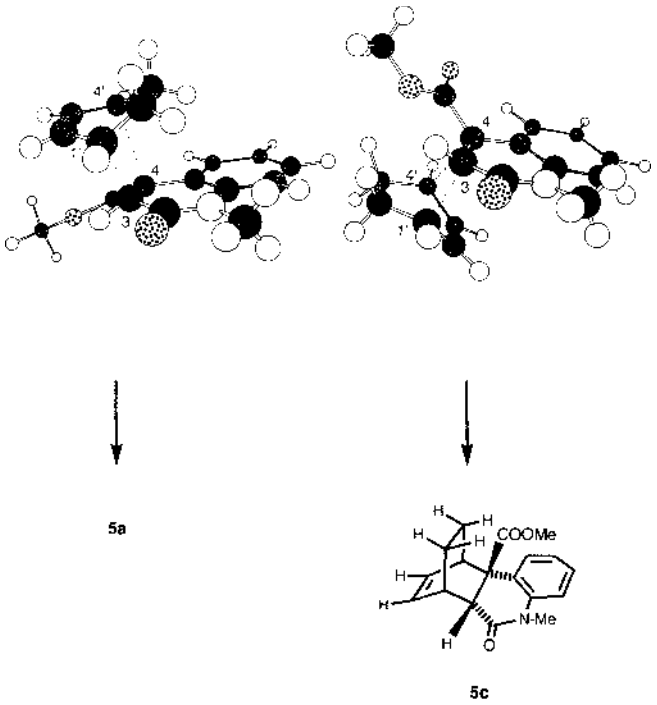

Fig. 2. Calculated Structures of TS for *Endo*-Addition (left) and for *Exo*-Addition (right) and the Corresponding Adducts in the DA Reactions of **1a** with **2c**

The calculated relevant interatomic distances are: $C_1 \cdot C_3 = 2.039$ Å, $C_4 \cdot C_4 = 2.427$ Å (left); $C_1 \cdot C_3 = 2.032$ Å, $C_4 \cdot C_4 = 2.432$ Å (right).

but **5c** was not experimentally obtained.

In conclusion, thermal DA reactions of 2(1*H*)-quinolones having an electron-withdrawing group at the 4-position with isoprene, butadiene sulfone and cyclohexadiene (**2a**—**c**) produced stereoselectively functionalized phenanthridones under AP and HP. The stabilization energy calculated using the AM1 method could predict the main products in these unsymmetrical DA reactions. The activation energy calculated by Gaussian 98 at RHF/6-31G (*d*) level was consistent with the experimental adducts of the DA reaction of **1a** with **2c**.

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-EX270 (^{1}H-NMR; 270 MHz, ^{13}C-NMR; 67.5 MHz) spectrometer with tetramethylsilane (TMS) as an internal standard; elemental analyses, Perkin Elmer 2400 CHN Elemental Analyzer. The following experimental conditions were used for chromatography; column chromatography, Merk Kieselgel Silica gel 60 (230—400 mesh); TLC, pre-coated TLC plates with $60F_{254}$ (2 mm, Merck).

General Procedure for DA Reactions of 1a—d with 2a A solution of **1a** (217 mg, 1 mmol) and **2a** (340 mg, 5 mmol) in *o*-xylene (3 ml) was heated at 180 °C for 5 d in a sealed tube, then the reaction mixture was concentrated *in vacuo*. The residue was fractionated by chromatography on a column of silica gel. The solvent of the first fraction that eluted with acetone–hexane (1 : 1) was evaporated. The crude product was purified by preparative TLC over silica gel with acetone–hexane (1 : 3) to give 5,6,6a,7,10,10a-hexahydro-*cis*-10a-methoxycarbonyl-5,8-dimethylphenanthridin-6-one (**3a**). The solvent of the second fraction that eluted with acetone–hexane (1 : 1) was evaporated and **1a** was recovered. The reactions of **1b**—**d** (1 mmol) with **2a** (5 mmol) were proceeded under the conditions listed in Table 1. The reaction mixture was manipulated in the same manner as described above to yield the corresponding crude products with recovery of the starting materials. The crude products were recrystallized from isopropyl ether or ether to give *cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-5,8-dimethylphenanthridin-6-one (**3b**), *cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-5,9-dimethylphenanthridin-6-one (**3e**), *cis*-10a-acetyl-5,6,6a,7,10,10a-hexahydro-5,8-dimethylphenanthridin-6-one (**3c**), *cis*-10a-acetyl-5,6,6a,7,10,10a-hexahydro-5,9-dimethylphenanthridin-6-one (**3f**), and *cis*-10a-benzoyl-5,6,6a,7,10,10a-hexahydro-5,8-dimethylphenanthridin-6-one (**3d**). The yields of **3a**—**f** are summarized in Table 1.

3a: Colorless needles (isopropyl ether), mp 110—113 °C. IR (KBr) cm^{-1}: 1729, 1678, 1605. ^{1}H-NMR ($CDCl_3$) δ: 1.66 (3H, s, C–Me), 2.13 (1H, dd, J=3.0, 18.0 Hz, H-7), 2.34 (1H, dd, J=2.0, 17.5 Hz, H-10), 2.52 (1H, d, J=17.5 Hz, H-10), 2.65 (1H, dd, J=5.0, 18.0 Hz, H-7), 3.34 (1H, dd, J=3.0, 5.0 Hz, H-6a), 3.37 (3H, s, N–Me), 3.76 (3H, s, O–Me), 5.36 (1H, d, J=2.0 Hz, H-9), 7.00—7.36 (4H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 23.3, 27.9, 29.9, 30.0, 41.5, 48.0, 52.7, 115.2, 118.0, 123.2, 125.3, 125.6, 128.4, 132.7, 139.2, 170.4, 173.9. MS *m/z*: 285 (M^+). *Anal.* Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71 ; N, 4.91. Found : C, 71.13; H, 6.78; N, 4.56.

3b: Colorless needles (ether), mp 120 °C. IR (KBr) cm^{-1}: 1702, 1669, 1601. ^{1}H-NMR ($CDCl_3$) δ: 1.82 (3H, s, C–Me), 2.34 (1H, dd, J=2.4, 18.0 Hz, H-10), 2.40 (1H, dd, J=2.4, 18.0 Hz, H-10), 2.50—2.59 (1H, m, H-7), 2.59 (1H, d, J=18.0 Hz, H-7), 3.09 (1H, d, J=5.9 Hz, H-6a), 3.39 (3H, s, N–Me), 5.33 (1H, br s, H-9), 7.05 (1H, dd, J=1.2, 8.1 Hz, H-4), 7.19 (1H, ddd, J=1.2, 7.6, 8.6 Hz, H-2), 7.40 (1H, ddd, J=1.5, 7.6, 8.1 Hz, H-3), 7.64 (1H, dd, J=1.5, 7.6 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 23.4, 27.6, 30.2, 33.1, 38.8, 41.8, 115.6, 116.0, 121.2, 123.8, 125.0, 126.2, 129.6, 140.0, 138.1, 167.3. MS *m/z*: 252 (M^+), 184 ($M^+ - C_5H_8$). HR-MS Calcd for $C_{16}H_{16}N_2O$: 252.1263. Found: 252.1287.

3e: Colorless needles (isopropyl ether), mp 200 °C. IR (KBr) cm^{-1}: 1702, 1669, 1601. ^{1}H-NMR ($CDCl_3$) δ: 1.56 (3H, s, C–Me), 2.27 (1H, d, J=18.5

Hz, H-10), 2.45 (1H, d, J=18.5 Hz, H-10), 2.52—2.64 (1H, m, H-7), 3.04 (1H, m, H-7), 3.11 (1H, d, J=6.4 Hz, H-6a), 3.35 (3H, s, N–Me), 5.58 (1H, br s, H-8), 7.06 (1H, dd, J=1.2, 8.3 Hz, H-4), 7.18 (1H, ddd, J=1.2, 7.6, 8.6 Hz, H-2), 7.41 (1H, ddd, J=1.5, 8.3, 8.6 Hz, H-3), 7.63 (1H, dd, J=1.5, 7.6 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 23.2, 23.4, 30.3, 37.2, 39.4, 40.9, 115.6, 120.3, 121.0, 123.8, 124.8, 126.1, 129.0, 140.0, 138.2, 167.4. MS *m/z*: 252 (M^+), 184 ($M^+-C_5H_8$). HR-MS Calcd for $C_{16}H_{16}N_2O$: 252.1263. Found: 252.1264.

3c: Colorless needles (ether), mp 108—109 °C. IR (KBr) cm^{-1}: 1707, 1665, 16001. ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3H, s, C–Me), 2.05 (3H, s, CO–Me), 2.14—2.19 (1H, br m, H-7), 2.34 (1H, d, J=17.8 Hz, H-10), 2.46 (1H, d, J=17.8 Hz, H-10), 2.58 (1H, dd, J=2.2, 17.6 Hz, H-7), 3.22 (1H, dd, J=2.2, 8.0 Hz, H-6a), 3.33 (3H, s, N–Me), 5.38 (1H, br s, H-9), 6.79—7.36 (4H, m, H-1, 2, 3, 4). ^{13}C-NMR ($CDCl_3$) δ: 23.0, 25.2, 28.6, 28.7, 29.7, 41.4, 52.8, 115.2, 117.1, 123.5, 125.5, 126.3, 128.6, 132.9, 140.1, 171.3, 207.4. MS *m/z*: 269 (M^+), 226. *Anal.* Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.62; H, 7.26; N, 5.16.

3f: Colorless needles (isopropyl ether), mp 140—141 °C. IR (KBr) cm^{-1}: 1702, 1669, 1601. ^{1}H-NMR ($CDCl_3$) δ: 1.74 (3H, s, C–Me), 2.07 (3H, s, CO–Me), 2.06—2.25 (2H, ddd, J=6.5, 7.6, 19.0 Hz, H-7,7), 2.33 (1H, d, J=17.5 Hz, H-10), 2.46 (1H, d, J=17.5 Hz, H-10), 3.15 (1H, dd, J=6.5, 7.6 Hz, H-6a), 3.33 (3H, s, N–Me), 5.32 (1H, br s, H-8), 7.03 (1H, d, J=8.1 Hz, H-4), 7.09 (2H, br s H-1,2), 7.33 (1H, t, J=8.1, 8.1 Hz, H-3). ^{13}C-NMR ($CDCl_3$) δ: 23.5, 24.2, 25.2, 29.7, 33.1, 40.6, 53.6, 115.2, 119.5, 123.4, 125.9, 128.6, 128.7, 130.4, 140.1, 171.3, 207.3. MS *m/z*: 269 (M^+), 226. HR-MS Calcd for $C_{17}H_{19}NO_2$: 269.1416. Found: 269.1405.

3d: Colorless needles (ether), mp 170—172 °C. IR (KBr) cm^{-1}: 1676, 1600. ^{1}H-NMR ($CDCl_3$) δ: 1.65 (3H, s, C–Me), 1.75 (1H, dd, J=4.0, 18.0 Hz, H-10), 2.17 (1H, dd, J=4.2, 16.3 Hz, H-7), 2.45 (1H, dd, J=4.2, 16.3 Hz, H-7), 2.84 (1H, dd, J=4.0, 18.0 Hz, H-10), 3.41 (3H, s, N–Me), 3.47 (1H, t, J=4.2, 4.2 Hz, H-6a), 5.93 (1H, br s, H-9), 7.01—7.55 (9H, m, H-aromatic, 1, 2, 3, 4). ^{13}C-NMR ($CDCl_3$) δ: 23.3, 27.0, 30.1, 31.0, 42.2, 52.0, 115.6, 118.3, 123.2, 126.9, 128.0, 128.1 (C2), 128.7, 129.4 (C2), 131.4, 132.0, 135.9, 139.1, 170.0, 201.0. MS *m/z*: 331 (M^+), 226. HR-MS Calcd for $C_{22}H_{21}NO_2$: 331.1573. Found: 331.1598.

General Procedure for DA Reactions of 1a—d with 2b A solution of **1a** (217 mg, 1 mmol) and **2b** (2.36 g, 20 mmol) in *o*-xylene (4 ml) was heated at 180 °C for 3 d in a sealed tube and the reaction mixture was concentrated *in vacuo*. The residue was fractionated by chromatography on a column of silica gel. The solvent of the first fraction that eluted with ethyl acetate–hexane (1 : 1) was evaporated. The crude product was purified by preparative TLC over silica gel with ethyl acetate to give 5,6,6a,7,10,10a-hexahydro-*cis*-10a-methoxycarbonyl-5-methylphenanthridin-6-one (**4a**). The solvent of the second fraction that eluted with ethyl acetate–hexane (1 : 1) was evaporated, and **1a** was recovered. The reactions of **1b**, **c** (1 mmol) with **2b** (20 mmol) proceeded under the conditions listed in Table 1 and the reaction mixtures were manipulated as described above to give *cis*-10a-cyano-5,6,6a,7,10,10a-hexahydro-5-methylphenanthridin-6-one (**4b**), and *cis*-10a-acetyl-5,6,6a,7,10,10a-hexahydro-5-methyl-phenanthridin-6-one (**4c**) with recovery of the respective starting materials. However, the reaction of **1d** (1 mmol) with **2b** (5 mmol) did not give the product (**4d**), and **1d** was recovered. The yields of **4a**—**c** are summarized in Table 1.

4a: Pale yellow plates (acetone–hexane), mp 84—87 °C. IR (KBr) cm^{-1}: 1722 , 1665, 1603. ^{1}H-NMR ($CDCl_3$) δ: 2.23 (1H, ddd, J=2.6, 5.3, 18.1 Hz, H-7), 2.37 (1H, dd, J=2.1, 17.8 Hz, H-10), 2.60—2.71 (2H, br m, H-7,10), 3.33 (1H, t, J=5.3, 5.3 Hz, H-6a), 3.38 (3H, s, N–Me), 3.77 (3H, s, O–Me), 5.65 (1H, d, J=12.0 Hz, H-8 or 9), 5.69 (1H, d, J=12.0 Hz, H-8 or 9), 7.00—7.08 (3H, m, H-1, 2, 4), 7.27—7.36 (1H, m, H-3). ^{13}C-NMR ($CDCl_3$) δ: 23.3, 29.7, 23.0, 40.9, 48.1, 52.7, 115.1, 123.0, 123.6, 125.1, 125.2 (C2), 128.3, 139.0, 170.0, 173.5. MS *m/z*: 271 (M^+), 212, 197, 184, 168. HR-MS Calcd for $C_{16}H_{17}NO_3$: 271.1208. Found: 271.1208. *Anal.* Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 71.08; H, 6.21; N, 4.87.

4b: Colorless columns (acetone–hexane), mp 149—150 °C. IR (KBr) cm^{-1}: 2239, 1670, 1599. ^{1}H-NMR ($CDCl_3$) δ: 2.34—2.46 (2H, br m, H-10), 2.52—2.68 (1H, m, H-7), 3.06—3.14 (2H, br m, H-6a, 7), 3.40 (3H, s, N–Me), 5.62—5.70 (1H, m, H-9), 5.91 (1H, ddd, J=2.5, 5.0, 10.0 Hz, H-8), 7.05 (1H, dd, J=1.2, 8.2 Hz, H-1), 7.19 (1H, ddd, J=1.2, 7.6, 7.7 Hz, H-3), 7.40 (1H, ddd, J=1.6, 7.6, 8.2 Hz, H-2), 7.63 (1H, dd, J=1.6, 7.6 Hz, H-4). ^{13}C-NMR ($CDCl_3$) δ: 23.0, 30.3, 32.7, 38.7, 41.3, 115.45, 120.7, 121.5, 123.6, 124.7, 125.8, 126.3, 129.4, 138.0, 166.9. MS *m/z*: 238 (M^+), 209, 184, 156, 128. HR-MS Calcd for $C_{15}H_{14}N_2O$: 238.1106. Found: 238.1144.

4c: Colorless columns (acetone–hexane), mp 132—134 °C. IR (KBr) cm^{-1}: 1703, 1680, 1600. ^{1}H-NMR ($CDCl_3$) δ: 2.06 (3H, s, CO–Me), 2.09—2.29 (2H, m, H-7), 2.42 (1H, ddd, J=2.8, 5.4, 18.1 Hz, H-10), 2.62 (1H, ddd, J=1.8, 3.9, 18.1 Hz, H-10), 3.23 (1H, dd, J=6.3, 8.0 Hz, H-6a), 3.33 (3H, s, N–Me), 5.58—5.64 (1H, br m, H-8), 5.66—5.74 (1H, br m, H-9), 7.02 (1H, dd, J=1.0, 8.1 Hz, H-4), 7.07—7.18 (2H, m, H-1,2), 7.33 (1H, ddd, J=1.8, 7.1, 8.1 Hz, H-3). ^{13}C-NMR ($CDCl_3$) δ: 24.0, 25.1, 28.3, 29.67, 40.8, 52.9, 115.0, 122.9, 123.2, 125.3, 125.4, 125.9, 128.5, 139.9, 170.9, 206.8. MS *m/z*: 255 (M^+), 212, 197, 184, 168. HR-MS Calcd for $C_{16}H_{17}NO_2$: 255.1259. Found: 255.1270. *Anal.* Calcd for $C_{16}H_{17}NO_2$: C, 75.27 ; H, 6.71 ; N, 5.49. Found: C, 75.11; H, 6.70; N, 5.41.

DA Reaction of 1a with 2c The reaction of **1a** (1 mmol) with **2c** (400 mg, 5 mmol) was proceeded under the conditions listed in Table 1 and the reaction mixture was concentrated *in vacuo*. The residue was fractionated by chromatography on a column of silica gel. The solvent of the first fraction eluted with acetone–hexane (1 : 1) was evaporated. The crude product was purified by preparative TLC over silica gel with acetone–hexane (1 : 3) to give *endo*-7,10-ethylene-*cis*-10a-methoxycarbonyl-5-methyl-5,6,6a,7,10,10a-hexahydrophenanthridin-6-one (**5a**) and *endo*-7,10-ethylene-*trans*-10a-methoxycarbonyl-5-methyl-5,6,6a,7,10,10a-hexahydrophenanthridin-6-one (**5b**), respectively. The solvent of the second fraction that eluted with acetone–hexane (1 : 1) was evaporated, and **1a** was recovered. The yields of **5a**, **b** are summarized in Table 1.

5a: Colorless columns (acetone–hexane), mp 139—140 °C. IR (KBr) cm^{-1}: 1732, 1652, 1597. ^{1}H-NMR ($CDCl_3$) δ: 1.01—1.36 (4H, m, H-11, 12), 3.16 (1H, d, J=7.6 Hz, H-6a), 3.28 (1H, dddd, J=2.5, 7.6, 9.6, 9.6 Hz, H-7), 3.38 (1H, ddd, J=2.3, 5.3, 7.9 Hz, H-10), 3.42 (3H, s, N–Me), 3.58 (3H, s, O–Me), 6.42—6.50 (2H, m, H-8,9), 7.00—7.09 (2H, m, H-aromatic), 7.27—7.32 (1H, m, H-aromatic), 7.46—7.49 (1H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 20.0, 20.1, 29.4, 34.6, 39.3, 46.2, 51.7, 52.6, 114.7, 122.3, 123.2, 127.8, 128.7, 134.2, 134.9, 138.7, 168.6, 175.3. MS *m/z*: 297 (M^+), 218. HR-MS Calcd for $C_{18}H_{19}NO_3$: 297.1365. Found: 297.1349.

5b: Colorless oil. IR (film) cm^{-1}: 1729, 1661, 1596. ^{1}H-NMR ($CDCl_3$) δ: 1.26—1.37 (2H, m, H-11, 12), 1.75—1.80 (2H, m, H-11,12), 3.25 (1H, ddd, J=1.6, 4.9, 7.9 Hz, H-7), 3.45 (1H, d, J=1.6 Hz, H-6a), 3.32 (3H, s, N–Me), 3.49—3.64 (1H, m, H-10), 3.67 (3H, s, O–Me), 5.92 (1H, ddd, J=1.3, 6.6, 8.3 Hz, H-9), 6.19 (1H, t, J=6.6, 6.6 Hz, H-8), 6.86 (1H, dd, J=1.0, 7.3 Hz, H-4), 7.01 (1H, ddd, J=1.0, 7.3, 7.3 Hz, H-2), 7.21 (1H, ddd, J=1.3, 7.3, 7.3 Hz, H-3), 7.59 (1H, dd, J=1.3, 7.3 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 20.0, 20.1, 29.4, 34.6, 39.3, 46.2, 51.7, 52.6, 114.7, 122.3, 123.2, 127.8, 128.7, 134.2, 134.9, 138.7, 168.6, 175.3. MS *m/z*: 297 (M^+), 218. HR-MS Calcd for $C_{18}H_{19}NO_3$: 297.1365. Found: 297.1336.

Treatment of 5a with LDA A solution of **5a** (160 mg, 0.54 mmol) in tetrahydrofuran (10 ml) was cooled to −78 °C. A 1.5 M hexane solution of LDA (0.43 ml, 0.65 mmol) was added to the cooled solution and stirred at the same temperature for 1.5 h. To the reaction mixture, MeOH (0.5 ml) was added, and after 5 min, saturated aqueous NH_4Cl (0.3 ml) was added. The mixture was stirred while warming to room temperature, and poured into 10% HCl (10 ml) and extracted with chloroform. The chloroform extract was washed with saturated aqueous NaCl (5 ml), dried over Na_2SO_4, and evaporated. The residue was purified by preparative TLC (ether–hexane= 1 : 4) to give **5b** (15 mg, 5%) with recovery of **5a**.

General Procedure for HP-DA Reactions of 1a—d with 2a and 2c a) A mixture of **1a** (108 mg, 0.5 mmole) and **2a** (170 mg, 2.5 mmol) in dichloromethane (2 ml) in a Teflon tube was placed in a HP reactor and pressurized to 5 kbar, then heated at 80 °C for 2 d. The pressure was released and the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography and by preparative TLC as described above to give **3a** with recovery of **1a**. The reactions of **1b**, **c** (0.5 mmol) with **2a** (2.5 mmol) proceeded under the conditions listed in Table 1 and the reaction mixtures were manipulated as described above to give **3b**, **c**. However, the reaction of **1d** (0.5 mmol) with **2b** (2.5 mmol) did not give the product (**4d**) and **1d** was recovered. b) The reaction of **1a** (0.5 mmol) with **2c** (200 mg, 2.5 mmol) proceeded under the condition listed in Table 1 and the mixture was manipulated as described above to give **5a**. The yields of **3a**—**c** and **5a** are summarized in Table 1.

Calculation of Activation Energy We optimized the structures of the initial state and the TS using the RHF/6-31G (d) basis set in the Gaussian 98 program package.[10] The effect of the solvent was not considered. Assuming that the diene and the dienophile were far apart at the initial state, we calculated the activation energy (*Ea*) as the difference in energy between the TS and the initial state. After optimizing the TS structure, we performed the vibrational calculation and confirmed that the TS had an imaginary vibrational frequency of exactly one. We also calculated the intrinsic reaction coordinate (IRC) to confirm that the TS connected the initial, with the intended final state.

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