Diels–Alder Cycloadditions of 2(1*H*)-Quinolones Having an Electron-Withdrawing Group at the 3-Position Acting as Dienophiles with Dienes

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Diels–Alder cycloadditions of 2(1*H*)-quinolones having an electron-withdrawing group at the 3-position with alkyl- and silyloxy-1,3-butadienes (2a, b) were carried out to give phenanthridones richly functionalized regio- or stereoselectively under conditions of atmospheric and high pressure. Furthermore, regioselectivity and chemoselectivity of 3-substituted 2(1*H*)-quinolones to 2a, b were examined using MO calculation.

Key words 3-substituted 2(1*H*)-quinolone; Diels–Alder cycloaddition; regioselectivity; chemoselectivity; electron-withdrawing group; MO calculation

2(1*H*)-Quinolones are aromatic and there are many reports of substitution reactions.[1)] Recently, Nakagawa and co-workers reported the first example of a Diels–Alder (DA) reaction of 1-methoxycarbonyl-3-phenylthio-2(1*H*)-quinolone with 2-silyloxydiene in the presence of Lewis acid gave the intermediate for the Dynemisine A core (a marine alkaloid) in 60—70% yield. The above thermal reactions with 2-silyloxydiene or Danishefsky diene were unsuccessful.[2)] The phenanthridone skeleton aromatized or hydrogenated is commonly found in many alkaloids[3)] of Amarylidaceae. Therefore, phenanthridones richly functionalized would be expected to be potentially valuable synthetic intermediates, and to possess interesting biological activities.[3)] We have also reported the synthesis of phenanthridones richly functionalized using DA cycloadditions of 2(1*H*)-quinolones having an electron-withdrawing group at the 4-position.[4)] It is considered that cycloadditions of 3-substituted 2(1*H*)-quinolones, a moiety acting as a dienophile give phenanthridones functionalized at different positions from those resulting from the DA cycloaddition of 4-substituted 2(1*H*)-quinolones. In this paper, we wish to report the synthesis of phenanthridones by uncatalyzed and thermal DA cycloadditions of 1-methyl-2(1*H*)-quinolones having an electron-withdrawing group at the 3-position with alkyl- and silyloxy-1,3-butadienes under atmospheric and high pressure (AP and HP[5)]) conditions.

DA Cycloaddition Firstly, DA cycloadditions of 1-methyl-2(1*H*)-quinolones having an electron-withdrawing group [such as methoxycarbonyl- (**1a**),[6)] cyano- (**1b**),[7)] acetyl- (**1c**), benzoyl- (**1d**),[1d,e)] formyl- (**1e**),[8)] and nitro- (**1f**, **g**),[9)]] at the 3-position with 2,3-dimethyl-1,3-butadiene (**2a**) were examined under AP conditions as shown in Table 1 and Chart 1. The reactions of **1a**—**d** with a symmetric diene (**2a**) gave stereoselectively functionalized phenanthridones (**3a**—**c**, **e**, entries 1, 3, 5, 7) at 180 °C in moderate yields, but that of **1d** afforded the adduct (**3d**, entry 6) in poor yield. Upon treatment with diisobutylaluminum hydride (DIBAL), the ester carbonyl group in **3a** was reduced to the hydroxymethyl group *i.e.* **4**. The same reactions of **1f** at 160 °C produced the *cis*-adduct (**3f**, entry 8) in 46% yield stereoselectively, and at 180 °C gave a new product (**5a**, entry 9) aromatized by elimination of HNO_2 and dehydrogenation in 95% yield. Similarly, the reaction of **1g** at 180 °C (neat) afforded the *cis*-adduct (**3g**, entry 10) in 94% yield and additional heating of **3g** at 180 °C for 2 d in *o*-xylene gave the aromatized product (**5b**) in 64% yield. HP-DA cycloadditions[5)] of **1a**, **b** with **2a** at 120 °C for 2 d afforded stereoselectively the *cis*-adducts [**3a** (51%), entry 2; **3b** (7%), entry 4] with the recovery of the starting material.

Furthermore, cycloadditions of **1a**, **b**, **e**, **f** with Danishefsky's diene (**2b**) were attempted under AP and HP conditions (Table 2, Chart 2). The reaction of **1a** with unsymmetric **2b** was carried out at 180 °C for 4 d, followed by trifluoroacetic acid (TFA) work-up to give the *cis*-enone adduct (**6a**, entry 1) in 93% yield, regio- and stereoselectively. Upon treatment with water, the above reaction mixture afforded regio- and stereoselectively the *cis*-methoxy adduct [**7a** (91%), entry 2] only. Under HP condition (10 kbar, 90 °C), the reaction of **1a** with **2b** afforded the *cis*-enone adduct [**6a** (62%), entry 3] and the new *cis*-methoxy adduct [**8a** (24%), entry 3]. The above reaction mixture was treated with water to give a mixture [**6a** (32%), **7a** (trace), **8a** (40%), entry 4]. Moreover, the reaction of **1b** with **2b** under AP condition afforded only the *cis*-enone adduct [**6b** (98%), entry 5], followed by refluxing with TFA in chloroform. The above reaction mixture was worked up with TFA at room temperature to give **6b** (66%), the *cis*-methoxy adduct (**7b**, 9%), and the *trans*-methoxy adduct [**8b** (9%), entry 6]. On the other hand, the HP reaction of **1b** with **2b** afforded mixture [**6b** (4%), **7b** (9%), **8b** (66%), entry 7]. Conversion of the methoxy adduct (**7a**) to **6a** using TFA proceeded smoothly, in order to reduce the steric hindrance between the methoxy and the ester groups, in 97% yield. On the other hand, conversion of the *cis*-methoxy adduct (**8a**) to **6a** proceeded more slowly than **7a** in 97% yield. Similarly, treatment of the *cis*-methoxy adduct (**7b**, **8b**) with TFA gave **6b** in 79% and 68% yields, respectively. As a result, **7a** and **8a** were isomeric with each other relating to the stereochemistry of the methoxy group and, in addition, **7b** and **8b** were also isomeric. Furthermore, the reaction of **1e** with **2b** produced chemoselectively the hetero DA adduct (**9**, entry 8) in 71% yield, resulting from 1,4-addition of the formyl group to **2b.**[10)] DA cycloaddition of **1f** with **2b** gave only the aromatic product [**10a** (40%), entry 9] which was the form favored by enolization of the enone product (**10b**), because of the important stability associated

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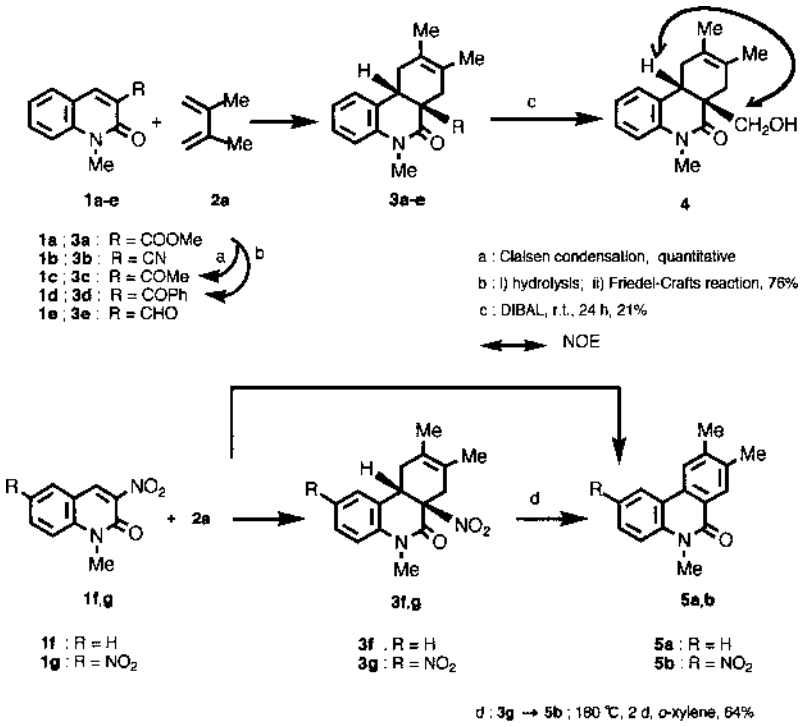

Chart 1

Table 1. DA Cycloadditions of **1a**—**g** with **2a**

Entry	Substrate	Temp. (°C)	Time (d)	Solvent	Pressure (kbar)	Adduct	Yield (%)
1	**1a**	180	3	*o*-Xylene	Atmospheric	**3a**	40
2	**1a**	120	2	CH_2Cl_2	10	**3a**	51
3	**1b**	180	4	*o*-Xylene	Atmospheric	**3b**	46
4	**1b**	120	2	CH_2Cl_2	10	**3b**	7
5	**1c**	180	3	*o*-Xylene	Atmospheric	**3c**	75
6	**1d**	180	3	*o*-XYlene	Atmospheric	**3d**	17
7	**1e**	180	3	*o*-Xylene	Atmospheric	**3e**	97
8	**1f**	160	3	*o*-Xylene	Atmospheric	**3f**	46
9	**1f**	180	3	*o*-Xylene	Atmospheric	**5a**	95
10	**1g**	180	3	Neat	Atmospheric	**3g**	94

with the aromatic system. The product (**10b**) was derived from the DA adduct (**10c**) by release of hydrogen and nitrogen dioxide (HNO_2).

Next, the stereochemistries of the ring juncture in **3a**—**f**, **6a**, **b**, **7a**, **b**, and **8a**, **b**, were examined by the following way. The stereochemistries of the methoxycarbonyl, methoxy groups and H-10a in **7a** were established by X-ray crystal structure determination (Fig. 1). This showed that the ring juncture in **7a** was *cis*. The *cis*-stereochemistry of the ring juncture in **6a** was determined by nuclear Overhauser effect (NOE) measurement of ^{1}H-NMR spectra. Thus, when H-10a in **6a** was irradiated, an NOE was observed between H-10a and methyl in the methoxycarbonyl group. It was determined that since both the demethanolations of **7a** and **8a** gave **6a**, that in **8a** was also *cis*, that is, those in **6a**, **7a** and **8a** were same. Similarly, the stereochemistries of those in **6b**, **7b** and **8b** were same. DA adducts were *cis*-forms according to the well-known Alder–Stein rule (*cis*-principle). In addition, in ^{1}H-NMR spectra, the signals due to H-10a in **6a**, **7a**, and **8a** were located at 3.92, 3.97 and 3.47 ppm, and those of **6b**, **7b**, and **8b** appeared at 3.85, 3.83 and 3.74 ppm. Based on the above facts, the stereochemistries of the ring juncture in **6b**, **7b**, and **8b** were deduced as *cis*. Moreover, the *cis*-stereochemistries of the ring juncture in **3a** and **3c**, **d** was determined by NOE measurement. Thus, when H-10a was irradiated in the reduced form (**4**) of **3a** mentioned above, an NOE was observed between H-10a and the methylene of the hydroxymethyl group. Similarly, the NOE of **3c**, **d** indicated the correlation between H-10a and the acetyl or formyl group. In ^{1}H-NMR spectra, the signals due to H-10a in **3a**, **c**, **d** were located at 3.45, 3.68 and 3.33 ppm and those in **3b**, **e**, **f** appeared at 3.33—3.99 ppm. From the these data, the stereochemistries of the ring juncture in **3b**, **e**, **f** were deduced as *cis*. The stereochemistries of between the methoxycarbonyl and methoxy groups in **7a**, **b** and **8a**, **b** were examined in the following way. That in **7a** was determined to be *cis* by X-ray crystal structure analysis as shown in Fig. 1. Since **7a**, **b** and **8a**, **b** were isomeric, that in **8a** was confirmed to be *trans*. The demethanolation of **7a**, **b** proceeded faster than that of **8a**, **b** to reduce the steric hindrance between the methoxycar-

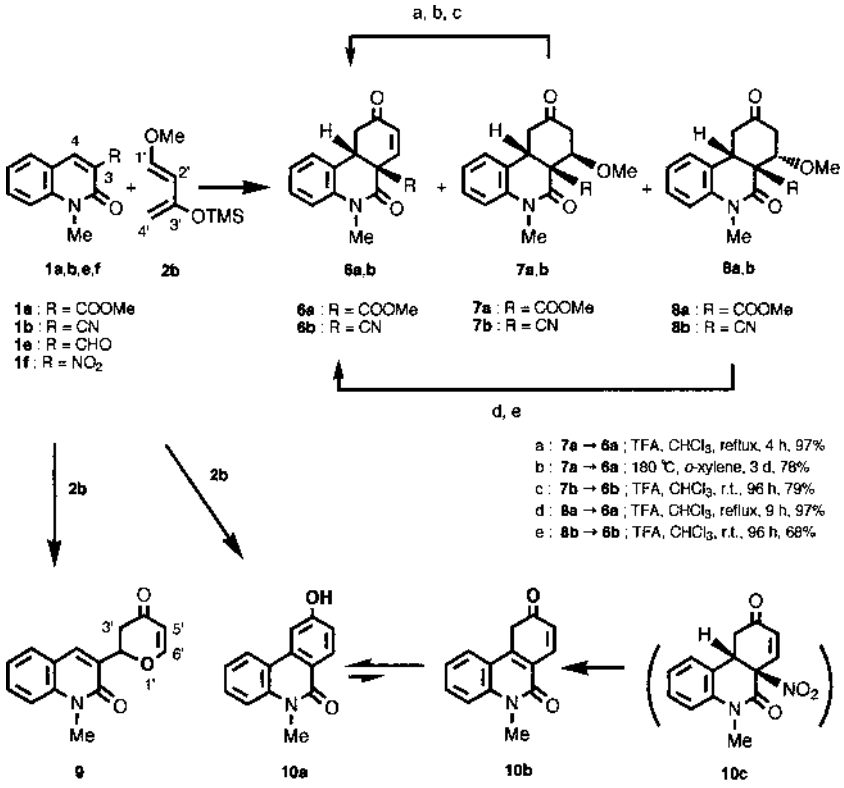

Chart 2

Table 2. DA Cycloadditions of **1a**, **b**, **e**, **f** with **2b**

Entry	Substrate	Temp. (°C)	Time (d)	Solvent	Pressure (kbar)	Work up ($CHCl_3$)	Adduct	Yield (%)
1	**1a**	180	4	*o*-Xylene	Atmospheric	TFA-r.t.	**6a**	93
2	**1a**	180	4	*o*-Xylene	Atmospheric	H_2O-r.t.	**7a**	91
3	**1a**	90	2	CH_2Cl_2	10	TFA-r.t.	**6a**	62
							8a	24
4	**1a**	90	2	CH_2Cl_2	10	H_2O-r.t.	**6a**	32
							7a	Trace
							8a	40
5	**1b**	180	3	*o*-Xylene	Atmospheric	TFA-reflux	**6b**	98
6	**1b**	180	3	*o*-Xylene	Atmospheric	TFA-r.t.	**6b**	66
							7b	9
							8b	9
7	**1b**	90	2	CH_2Cl_2	10	TFA-r.t.	**6b**	4
							7b	9
							8b	66
8	**1e**	160	2	*o*-Xylene	Atmospheric	TFA-r.t.	**9**	71
9	**1f**	180	3	*o*-Xylene	Atmospheric	TFA-r.t.	**10a**	40

bonyl and methoxy groups. Based on the above facts, it was deduced that the stereochemistry of **7b** was *cis* and that of **8b** was trans.

Regio-, Chemo-, and Stereoselectivity Since the diene and the dienophiles are unsymmetric in the DA reactions of **1a**, **b**, and **1f** with **2b**, regioisomers would be produced. In the present experiments, only the products from the (1′-3,4′-4)-addition reactions were obtained. (The numbers of atoms are indicated in Chart 2.) But in the DA reaction of 4-substituted 2(1*H*)-quinolones with **2b**, only the adducts from (1′-4,4′-3)-addition reactions were produced.[4] We studied this regioselectivity theoretically using the stabilization energy (ΔE) expressed by Eq. 1 in ref. 4 as a reaction index. We optimized **1a**, **b**, **f**, **1a**′, and **2b** using the semi-empirical molecular orbital PM3 method.[11] Then we calculated ΔE considering only HOMO of the diene and LUMO of the dienophile. Table 3 summarizes the calculated values of ΔE together with the experimentally obtained products. As is seen from Table 3, the calculated values of ΔE are consistent with the experimentally obtained products.

It is very interesting that the DA reaction of **1e** with **2a** produced the phenanthridone (**3e**) but did not form the adduct bearing a pyran ring. Whereas, the DA reaction of **1e** with **2b** gave **9** having a pyran ring but did not afford the phenanthridone. To study these differences theoretically, we searched and optimized the structures of transition states (TS) of the reactions using Gaussian 98 at RHF/6-31++G(*d*,*p*)//RHF/6-31G(*d*) level.[13] 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 the activation energy (*Ea*). In Table 4, we summarize the calculated activation energies of these four reactions together with the experimental yields of adducts (**3e**, **9**). We can see that *Ea* of the 3,4-addition for the reaction with **2a** is smaller than that of the HC=O addition. On the other hand, *Ea* of the HC=O addition for the reaction with **2b** is smaller than that of the 3,4-addition. These results are consistent with the experimental yields of the adducts (**3e**, **9**).

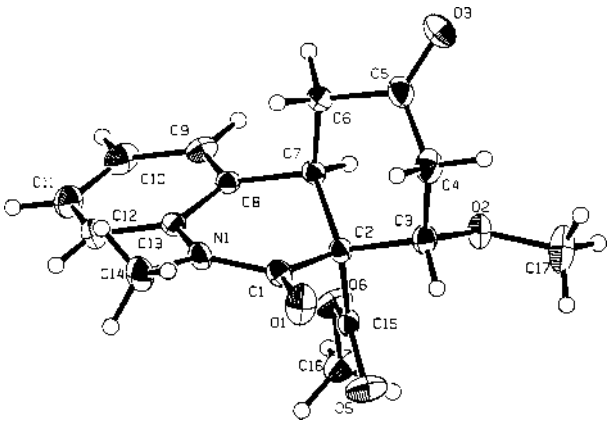

Fig. 1. ORTEP Drawing of **7a**

Table 3. Regioselectivity Based on the Stabilization Energy (ΔE) Caluclated Using PM3 Method

Substrate	Diene	(1′-3,4′-4) Addition[a]		(1′-4,4′-3) Addition[a]	
		$\Delta E/\gamma^2$	Adduct	$\Delta E/\gamma^2$	Adduct
1a	**2b**	0.0865	**6a**, **7a**, **8a**	0.0819	—
1b	**2b**	0.0925	**6b**, **7b**, **8b**	0.0868	—
1f	**2b**	0.0964	**10a**	0.0873	—
1a′[b]	**2b**	0.0623	—	0.0647	**7a′**[c]

a) The numbers of atoms are indicated in Chart 2. *b*) **1a′**: 4-methoxycarbonyl-2(1*H*)-qunolone.[4] *c*) **7a′**: adduct from **1a′**.[4]

Table 4. Experimental Yields of Adducts and Calculated Activation Energies for DA Cycloadditions of **1e** with **2a**, **b**

Diene	**1e**			
	3,4-Addition		HC=O addition	
	Ea[a] (kcal/mol)	Adduct (yield %)	*Ea*[a] (kcal/mol)	Adduct (yield %)
2a	43.04	97	48.98	—
2b	32.34	—	31.37	71

a) Calculated activation energy in unit of kcal/mol.

In the DA reactions of **1a** and **1b** with **2b**, the different stereoisomers were produced according to the reaction pressures (Table 2). To study this stereoselectivity, we searched and optimized the structures of TS and calculated the energies of the initial states and TS using Gaussian 98 at RHF/6-31G(*d*) level.[12] We display the structures of TS in the DA reactions of **1a** with **2b** in Fig. 2: TS(A) which would produce **7a** (left) and TS(B) which would produce **8a** (right). Table 5 summarizes the calculated values of the activation energies (*Ea*) and the corresponding adducts. The values of *Ea* are consistent with the adducts produced under AP (1 bar). However, the volume of TS will affect the rate of DA reaction under HP (10 kbar). We calculated the volumes of the molecules as the region within the 0.001 e/bohr^3 density envelope (1 bohr=0.529 Å). The calculate activation volume (*Va*) of TS(A) has -20.2 A^3 and that of TS(B) has -38.1 A^3. The value of *pVa* at $p=10$ kbar for TS(A) is -2.93 kcal/mol and that for TS(B) becomes -14.67 kcal/mol. The values of *pVa* at $p=1$ bar are practically zero. Then we can obtain the activation enthalpy (*Ha*) of the reaction by the following formula:

$$Ha=Ea+pVa$$

The calculated values of *Ha* are also listed in Table 5. The values of *Ha* are consistent with the experimental adducts under HP. Thus we can explain the adducts obtained under both AP and HP conditions in terms of the values of *Ha.* As

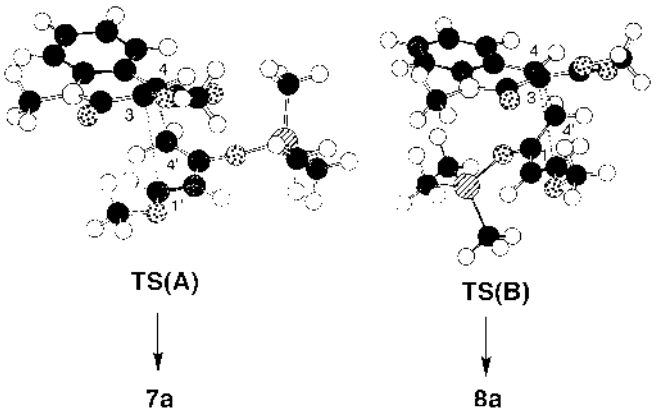

Fig. 2. Calculated Structures of TS in the DA Reactions of **1a** with **2b**: TS(A) Which Would Produce **7a** (Left) and TS(B) Which Would Produce **8a** (Right)

The calculated relevant interatomic distances are: C_1·C_3=3.181 Å, C_4·C_4=1.993 Å (left); C_1·C_3=3.097 Å, C_4·C_4=1.960 Å (right).

Table 5. Stereoselectivity in the DA Reaction of **1a** and **1b** with **2b**. Activation Energies (*Ea*) and Enthalpies (*Ha*) Were Calculated Using RHF/6-31G (d) Basis Set

Dienophile	Diene	Pressure	*via* TS(A)			*via* TS(B)		
			Ea (kcal/mol)	*Ha* (kcal/mol)	Adduct (yield %)	*EA* (kcal/mol)	*Ha* (kcal/mol)	Adduct (yield %)
1a	**2b**	1 atm	29.54	29.54	**7a** (91%)	31.26	31.26	—
		10 kbar	29.54	26.61	—	31.26	25.78	**8a** (24%)
1b	**2b**	1 atm	32.91	32.91	**7b** (12%)	33.62	33.62	**8b** (6%)
		10 kbar	32.91	30.19	**7b** (9%)	33.62	28.52	**8b** (66%)

is seen from Table 2, the yields of adducts under HP are comparable with those under AP, although the reactions under HP were performed at the lower temperature and the shorter reaction time. We can understand this fact by considering that the DA reactions were accelerated under HP because of the negative values of *Va* and consequently the smaller values of *Ha*.

In conclusion, thermal DA cycloadditions of 3-substituted 2(1*H*)-quinolones having an electron-withdrawing group (such as COOMe, CN, COMe, COPh, NO_2) with alkyl- and silyloxy-1,3-butadienes (**2a**, **b**) produced phenanthridones richly functionalized regio- or stereoselectively under AP and HP conditions and the reactions of 3-nitro-2(1*H*)-quinolones with **2a**, **b** gave aromatized phenanthridones. Moreover, regioselectivity of 3-substituted 2(1*H*)-quinolones to **2b** was examined by stabilization energy (ΔE) using semi-empirical MO calculation. Further, DA reactions of 3-formyl-2(1*H*)-quinolone with **2a**, **b** afforded chemoselectively a phenanthridone or the hetero DA adduct in fairly good yield and these results were supported by the activation energy (*Ea*) using *ab initio* MO calculation.

Experimental

The following instruments were used to obtain physical data: Melting points, Yanaco micro-melting point apparatus (values are uncorrected); IR spectra, Perkin Elmer ET-IR 1725X spectrometer; MS, JEOLJMS-DX 303/JMA-DA5000 spectrometer; NMR spectra, JNM-XX 600 MHz, JNM-GSX400 (^{1}H-NMR; 400 MHz, ^{13}C-NMR; 100 MHz), JNM-EX270 (^{1}H-NMR; 270 MHz, ^{13}C-NMR; 67.5 MHz), JEOLJNM-PMX 60$_{SI}$ 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).

Synthesis of 3-Acetyl-1-methyl-2(1*H*)-quinolone (1c) After a solution of 3-methoxycarbonyl-1-methyl-2(1*H*)-quinolone (**1a**, 2.17 g, 10 mmol) and sodium methoxide (801 mg, 15 mmol) in 20 ml ethyl acetate was stirred for 7 h while refluxing in an oil bath, conc-HCl (30 ml) and water (60 ml) were added. The acidic solution was refluxed for 3 h, basified with K_2CO_3 and extracted with chloroform. The chloroform extract was dried over Na_2SO_4, and evaporated to give **1c** (2.0 g, quantitative).

1c: Pale yellow plates (acetone), mp 110—114 °C. IR (KBr) cm^{-1}: 1678, 1653, 1611. ^{1}H-NMR ($CDCl_3$) δ: 2.77 (3H, s, COMe), 3.76 (3H, s, Me–N), 7.28 (1H, ddd, *J*=1.0, 7.8, 7.8 Hz, H-6 or 7), 7.38 (1H, d, *J*=8.1 Hz, H-5 or 8), 7.64—7.72 (2H, m, H-5 or 8, 6 or 7), 8.40 (1H, s, H-4). ^{13}C-NMR ($CDCl_3$) δ: 29.60, 31.00, 114.03, 119.14, 122.46, 128.89, 130.98, 132.88, 141.34, 142.32, 160.47, 197.99. MS *m*/*z*: 201 (M^+), 186. HR-MS *m*/*z*: Calcd for $C_{12}H_{11}NO_2$, 201.0790. Found: 201.0789.

Synthesis of 3-Benzoyl-1-methyl-2(1*H*)-quinolone (1d) A suspension of 1-methyl-2(1*H*)-quinolone-3-carboxylic acid (2.03 g, 10 mmol) hydrolyzed **1a** and thionyl chloride (3.57 g, 30 mmol) was refluxed for 3 h, and evaporated *in vacuo.* The solution of the residue in 30 ml benzene and $AlCl_3$ (2.67 g, 20 mmol) was refluxed for 6 h, and made basic with 10% NaOH. The benzene layer was dried over Na_2SO_4 and evaporated *in vacuo.* The residue was chromatographed on a column of alumina. The solvent of the fraction eluted with acetone–hexane (1 : 3) was evaporated to give **1d** (2.0 g, 76%).[8)]

General Procedure for DA Cycloadditions of 1a, 3-Cyano-1-methyl-2(1*H*)-quinolone (1b), 1c, 1d, 3-Formyl-1-methyl-2(1*H*)-quinolone (1e), 1-Methyl-3-nitro-2(1*H*)-quinolone (1f), 1-Methyl-3,6-dinitro-2(1*H*)-quinolone (1g) with 2a The solution of **1a** (217 mg, 1 mmol) and **2a** (410 mg, 5 mmol) in *o*-xylene (3 ml) was heated at 180 °C for 3 d in a sealed tube and the reaction mixture was concentrated *in vacuo.* The residue was chromatographed on a column of silica-gel. The solvent of the fraction eluted with acetone–hexane (1 : 2) was evaporated. The crude product was purified by preparative TLC over silica-gel with acetone–hexane (1 : 3) to give *cis*-5,6,6a,7,10,10a-hexahydro-6a-methoxycarbonyl-5,8,9-trimethylphenanthridin-6-one (**3a**). The reactions of **1b**—**g** (1 mmol) with **2a** (5 mmol) were carried out under the conditions listed in Table 1 and the crude products were purified using the same procedure as described above to give *cis*-6a-cyano-5,6,6a,7,10,10a-hexahydro-5,8,9-trimethylphenanthridin-6-one (**3b**), *cis*-6a-acetyl-5,6,6a,7,10,10a-hexahydro-5,8,9-trimethylphenanthridin-6-one (**3c**), *cis*-6a-benzoyl-5,6,6a,7,10,10a-hexahydro-5,8,9-trimethylphenanthridin-6-one (**3d**), *cis*-6a-formyl-5,6,6a,7,10,10a-hexahydro-5,8,9-trimethylphenanthridin-6-one (**3e**), *cis*-5,6,6a,7,10,10a-hexahydro-6a-nitro-5,8,9-trimethylphenanthridin-6-one (**3f**), *cis*-5,6,6a,7,10,10a-hexahydro-2,6a-dinitro-5,8,9-trimethylphenanthridin-6-one (**3g**), 5,8,9-trimethylphenanthridin-6-one (**5a**), respectively. The yields of **3a**—**g** and **5a** are summarized in Table 1.

3a: Colorless columns (acetone–hexane), mp 139—141 °C. IR (KBr) cm^{-1}: 1729, 1678, 1605. ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3H, s, Me–C), 1.68 (3H, s, Me–C), 1.99 (1H, dd, *J*=18.2, 10.9 Hz, H-10), 2.15 (1H, dd, *J*=18.2, 6.6 Hz, H-10), 2.38 (1H, d, *J*=17.0 Hz, H-7), 2.93 (1H, d, *J*=17.0 Hz, H-7), 3.41 (3H, s, Me–N), 3.45 (1H, dd, *J*=6.6, 10.9 Hz, H-10a), 3.51 (3H, s, COOMe), 6.97—7.04 (2H, m, H-aromatic), 7.16—7.28 (2H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 18.6, 18.7, 30.3, 34.7, 35.2, 38.4, 52.6, 53.6, 115.0, 122.9, 123.3, 123.6, 127.3, 127.7, 129.2, 138.6, 167.9, 172.7. MS *m*/*z*: 299 (M^+), 240, 217. *Anal.* Calcd for $C_{18}H_{21}NO_3$: C, 72.21; H, 7.07; N, 4.68. Found: C, 73.32; H, 7.12; N, 4.55.

3b: Colorless columns (acetone–hexane), mp 172—173 °C. IR (KBr) cm^{-1}: 2233, 1681, 1607. ^{1}H-NMR ($CDCl_3$) δ: 1.62 (3H, s, Me–C), 1.67 (3H, s, Me–C), 2.14 (1H, dd, *J*=9.3, 17.5 Hz, H-10), 2.30 (1H, dd, *J*=5.3, 17.5 Hz, H-10), 2.49 (1H, d, *J*=17.2 Hz, H-7), 2.97 (1H, d, *J*=17.2 Hz, H-7), 3.43 (3H, s, Me–N), 3.33 (1H, dd, *J*=5.3, 9.3 Hz, H-10a), 7.06—7.38 (4H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 18.4, 18.8, 30.9, 33.6, 35.0, 39.1, 42.3, 115.6, 119.4, 122.4, 123.3, 124.1, 127.0, 127.3, 128.6, 138.3, 163.4. MS *m*/*z*: 266 (M^+), 184. *Anal.* Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.51. Found: C, 76.88; H, 6.81; N, 10.48.

3c: Colorless powder (ether), mp 130—131 °C. IR (KBr) cm^{-1}: 1709, 1669, 1604. ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3H, s, Me–C), 1.69 (3H, s, Me–C), 1.93—2.27 (3H, m, H-7, 10, 10), 2.04 (3H, s, COMe), 2.95 (1H, d, *J*=17.0 Hz, H-7), 3.39—3.68 (1H, m, H-10a), 3.42 (3H, s, Me–N), 6.95—7.05 (2H, m, H-aromatic), 7.18—7.26 (2H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 18.6, 18.72, 26.2, 30.2, 34.8, 35.2, 37.3, 59.6, 115.1 123.4 (C2), 123.5, 127.5, 127.7, 129.9 (C2), 138.3, 169.1, 205.8. MS *m*/*z*: 283 (M^+), 240, 224, 198. HR-MS *m*/*z*: Calcd for $C_{18}H_{21}NO_2$ (M^+): 283.1572. Found: 283.1608. *Anal.* Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.65; H, 7.76; N, 4.89.

3d: Colorless needles (ether–hexane), mp 127—1219 °C. IR (KBr) cm^{-1}: 1681, 1665, 1604, 1416, 697. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (3H, s, Me–C), 1.71 (3H, s, Me–C), 2.06—2.20 (2H, br m, *J*=6.4, 17.6 Hz, H-10, 102.44 (1H, d, *J*=17.0 Hz, H-7), 3.10 (1H, d, *J*=17.0 Hz, H-7), 3.25 (3H, s Me–N), 3.67 (1H, dd, *J*=6.4, 10.4 Hz, H-10a), 6.77 (1H, dd, *J*=1.1, 8.1 Hz, H-4), 7.00 (1H, ddd, *J*=1.0, 7.9, 7.9 Hz, H-2), 7.14—7.19 (2H, br m, H-1, 3), 7.26—7.32 (2H, br m, H-3′, 5′), 7.43 (1H, dd, *J*=1.5, 8.5 Hz, H-4′), 7.57—7.60 (2H, br m, *J*=1.5, 8.5 Hz, H-2′, 6′). ^{13}C-NMR ($CDCl_3$) δ: 18.7, 18.9, 20.4, 34.5, 36.0, 39.0, 58.7, 115.0, 122.8, 123.4, 123.9, 127.4, 127.5, 127.9 (C2), 128.0 (C2), 130.0, 131.9, 137.5, 138.6, 169.5, 200.5. MS *m*/*z*: 345 (M^+), 240,172. HR-MS *m*/*z*: Calcd for $C_{23}H_{23}NO_2$ (M^+): 345.1729. Found: 345.1722.

3e: Colorless needles (ether–hexane), mp 114 °C. IR (KBr) cm^{-1}: 1731, 1674, 1605. ^{1}H-NMR ($CDCl_3$) δ: 1.61 (3H, s, Me–C), 1.70 (3H, s, Me–C), 2.04—2.16 (2H, m, H-10, 10), 2.21 (1H, d, *J*=17.0 Hz, H-7), 2.75 (1H, d, *J*=17.0 Hz, H-7), 3.33 (1H, dd, *J*=6.5, 10.0 Hz, H-10a), 3.42 (3H, s, Me–N), 6.98—7.07 (2H, m, 2, H-4), 7.18 (1H, dd, *J*=1.4, 7.5 Hz, H-1), 7.24—7.30 (1H, dd, *J*=1.8, 7.1 Hz, H-3), 9.37 (1H, s, CHO). ^{13}C-NMR ($CDCl_3$) δ: 18.6, 18.8, 30.2, 30.9, 34.4, 36.0, 57.7, 115.2, 122.8, 123.5, 123.5, 127.2, 127.8, 128.2, 138.7, 167.7, 198.3. MS *m*/*z*: 269 (M^+), 251, 240, 198. HR-MS *m*/*z*: Calcd for $C_{17}H_{19}NO_2$ (M^+): 269.1416. Found: 269.1407.

3f: Colorless powder (ether–acetone), mp 162—165 °C. IR (KBr) cm^{-1}: 1650, 1606, 1546, 1381. ^{1}H-NMR ($CDCl_3$) δ: 1.61 (3H, s, Me–C), 1.71 (3H, s, Me–C), 2.06 (1H, dd, *J*=10.5, 18.1 Hz, H-10), 2.38 (1H, dd, *J*=6.7, 18.1 Hz, H-10), 2.75 (1H, d, *J*=16.8 Hz, H-7), 3.21 (1H, d, *J*=16.8 Hz, H-7), 3.48 (3H, s, Me–N), 3.86 (1H, dd, *J*=6.7, 10.5 Hz, H-10a), 7.03—7.09 (2H, m, H-1, 3), 7.18 (1H, dd, *J*=1.7, 7.5 Hz, H-4), 7.26—7.33 (1H, m, H-2). ^{13}C-NMR ($CDCl_3$) δ: 18.4, 18.5, 30.6, 35.7, 36.4, 40.1, 91.1, 115.5, 122.8, 123.1, 124.0, 126.2, 127.7, 128.6, 137.8, 161.9. MS *m*/*z*: 286, 240 (M^+-NO_2), 224, 172. HR-MS *m*/*z*: Calcd for $C_{16}H_{18}N_2O_3$: 286.1317. Found: 286.1292.

3g: Colorless needles (ether), mp 180 °C. IR (KBr) cm^{-1}: 1549, 1372, 1522, 1342, 1615, 1597. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (3H, s, Me–C), 1.73 (3H, s, Me–C), 2.07 (1H, dd, *J*=11.0, 18.0 Hz, H-10), 2.47 (1H, dd, *J*=7.0, 18.0 Hz, H-10), 2.80 (1H, d, *J*=17.0 Hz, H-7), 3.54 (3H, s, Me–N), 3.99

(1H, dd, J=7.0, 11.0 Hz, H-10a), 7.16 (1H, d, J=9.0 Hz, H-4), 8.10 (1H, d, J=2.6 Hz, H-1), 8.21 (1H, J=2.6, 9.0 Hz, H-3). ^{13}C-NMR ($CDCl_3$) δ: 18.4, 18.5, 31.1, 35.3, 36.1, 40.0, 90.4, 115.7, 122.8, 122.9, 123.3, 124.6, 127.1, 143.1, 143.5, 161.9. MS *m/z*: 285 (M^+-NO_2), 239, 217. HR-MS *m/z*: Calcd for $C_{16}H_{17}N_2O_3$ (M^+-NO_2): 285.1239. Found: 285.1265.

5a: Pale yellow needles (ether), mp 212—213 °C. IR (KBr) cm^{-1}: 1651, 1619, 789, 739. ^{1}H-NMR ($CDCl_3$): 2.42 (3H, s, Me–C), 2.45 (3H, s, Me–C), 3.79 (3H, s, Me–N), 7.25—7.49 (2H, m, H-aromatic), 7.47—7.49 (1H, m, H-aromatic), 7.51 (1H, dd, J=1.5, 7.9 Hz, H-aromatic), 7.99 (1H, s, H-10), 8.22 (1H, dd, J=1.5, 7.9 Hz, H-aromatic), 8.27 (1H, s, H-7). ^{13}C-NMR ($CDCl_3$) δ: 19.7, 20.5, 29.83, 114.8, 119.2, 122.1 (C2), 122.7, 123.4, 128.7, 128.9, 131.2, 137.1, 137.7, 141.8, 161.5. MS *m/z*: 237 (M^+), 222, 206, 194. HR-MS *m/z* : Calcd for $C_{16}H_{15}NO$ (M^+): 237.1154. Found: 237.1150.

Heating of 3g The solution of **3g** (33 mg, 0.12 mmol) in 2 ml *o*-xylene was heated at 180 °C for 2 d and then concentrated *in vacuo.* The residue was purified by preparative TLC over silica gel with hexane–acetone (1 : 3) to give 5,8,9-trimethyl-2-nitrophenanthridin-6-one [**5b**, 18 mg, (64%)].

5b: Pale yellow needles (acetone), mp 270 °C. IR (KBr) cm^{-1}: 1661, 1609, 1519, 1335. ^{1}H-NMR ($CDCl_3$) δ: 2.55 (3H, s, C–Me), 2.62 (3H, s, Me–C), 4.08 (3H, s, Me–N), 7.83 (1H, d, J=9.5 Hz, H-4), 8.29 (1H, s, H-7 or 10), 8.32 (1H, s, H-7 or 10), 8.52 (1H, dd, J=2.4, 9.5 Hz, H-3), 9.34 (1H, d, J=2.4 Hz, H-1). ^{13}C-NMR ($CDCl_3$) δ: 20.4, 21.2, 33.1, 119.2, 123.2, 123.7, 124.8, 125.3, 125.9, 130.7, 133.2, 142.9, 125.3, 130.7, 133.2, 142.9, 143.2, 145.6, 148.7, 163.5. MS *m/z*: 282 (M^+), 252, 236. HR-MS *m/z*: Calcd for $C_{16}H_{14}N_2O_3$ (M^+): 282.1034. Found: 282.1035.

Reduction of 3a The solution of **3a** (37 mg, 0.124 mmol) in toluene 10 ml was stirred at −78 °C for 10 min and then DIBAL (0.3 ml, 1 mol/l) was added to the cooled solution. After being stirred at the same temperature for 30 min, the mixture was stirred for 24 h at room temperature. To the reaction mixture, MeOH (0.5 ml) was added and, after 30 min, the mixture was filtered. The organic layer was concentrated *in vacuo*, and the residue was chromatographed on a column of silica-gel. The solvent of the fraction eluted with hexane–acetone (4 : 1) was evaporated to give *cis*-5,6,6a,7,10, 10a-hexahydro-6a-hydroxymethyl-5,8,9-trimethylphenanthridin-6-one [**4**, 7 mg, (21%)].

4: Colorless columns (acetone–hexane), mp 128—130 °C. IR (KBr) cm^{-1}: 3403, 1649, 1602. ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3H, s, Me–C), 1.63 (3H, s Me–C), 1.99 (1H, d, J=18.0 Hz, H-7), 2.26—2.29 (2H, br m, H-10, 10), 2.36 (1H, d, J=18.0 Hz, H-7), 3.10 (1H, dd, J=6.6, 6.6 Hz, H-10a), 3.38 (3H, s, Me–N), 3.62 (1H, d, J=6.5 Hz, CH_2–O), 3.66 (1H, d, J=6.5 Hz, CH_2–O), 6.97—7.28 (4H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 18.8, 18.9, 30.0, 32.7, 33.0, 35.5, 46.0, 65.6, 114.5, 122.5, 123.4, 124.2, 126.6, 127.4, 128.5, 139.0, 173.2. MS *m/z*: 271 (M^+), 240, 189. *Anal.* Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.39; H, 8.00; N, 4.96.

General Procedure for DA Cycloadditions of 1a, b, e, f with 2b a) The solution of **1a** (217 mg, 1 mmol) and **2b** (860 mg, 5 mmol) in *o*-xylene (3 ml) was heated at 180 °C for 4 d in a sealed tube. The reaction mixture was concentrated *in vacuo* and diluted with chloroform. To reaction mixture, TFA (1 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 the second fraction eluted with acetone–hexane (1 : 2) was evaporated. The crude product was purified by a preparative TLC over silica gel with ether–hexane (4 : 1) to give *cis*-5,6,6a,7,8,10a-hexahydro-10a-methoxycarbonyl-5-methyl-6,9-dioxophenanthridine (**6a**). b) To the same reaction mixture, water (2 ml) was added with stirring at room temperature for 20 min. The chloroform layer was dried over $MgSO_4$ and concentrated *in vacuo.* The residue was chromatographed on a column of silica-gel. The solvent of the second fraction eluted with acetone–hexane (1 : 2) was evaporated. The crude product was rechromatographed on a column of silica-gel with ether–hexane (4 : 1) to give **6a** and *cis*-5,6,6a,7,8,9,10,10a-octahydro-*r*-10-methoxy-*c*-6a-methoxycarbonyl-5-methylphenanthridin-6,9-dione (**7a**). The second fraction gave *cis*-5,6,6a,7,8,9,10,10a-octahydro-*r*-10-methoxy-*t*-6a-methoxycarbonyl-5-methylphenanthrid-in-6,9-dione (**8a**). c) The reactions of **1b**, **e** (1 mmol) with **2b** (5 mmol) were carried out under the conditions listed in Table 2 and the crude products were purified using the same procedure as described above to give *cis*-6a-cyano-5,6,6a,7,8,10a-hexahydro-5-methylphenanthridin-6,9-dione (**6b**), *cis*-6a-cyano-5,6,6a,7,8,10a-hexahydro-*c*-7-methoxy-5-methylphenanthridin-6,9-dione (**7b**), *cis*-6a-cyano-5,6,6a,7,8,10a-hexahydro-*t*-methoxy-5-methylphenanthridin-6,9-dione (**8b**), 3-(2,3-dihydro-4*H*-pyran-4-one-2-yl)-1-methyl-2(1*H*)-quinolone (**9**), 9-hydroxy-5-methyl- phenanthridin-6-one (**10a**), respectively. The yields of **6a**, **b**, **7a**, **b** **8a**, **b**, **9**, and **10a** are summarized in Table 2.

6a: Colorless columns, mp 136—138 °C (acetone–ether). IR (KBr) cm^{-1}: 1736, 1686, 1668, 1603. ^{1}H-NMR ($CDCl_3$) δ: 2.17—2.70 (2H, m, J=5.8, 11.0, 16.8 Hz, CH_2), 3.45 (3H, s, Me–N), 3.67 (3H, s, COOMe), 3.92 (1H, dd, J=5.8, 11.0 Hz, H-10a), 6.22 (1H, d, J=10.2 Hz, H-7), 7.05—7.36 (5H, m, H-8, aromatic). ^{13}C-NMR ($CDCl_3$) δ: 30.3, 40.5 (C2), 53.5, 55.5, 115.4, 124.2, 125.0, 127.6, 128.8, 130.3, 138.5, 145.3, 165.3, 170.0, 195.4. MS *m/z*: 285 (M^+), 226. *Anal.* Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.58; H, 5.31; N, 4.64.

7a: Colorless columns, mp 155—157 °C (acetone–hexane). IR (KBr) cm^{-1}: 1738, 1717, 1681, 1605. ^{1}H-NMR ($CDCl_3$) δ: 2.32 (1H, d, J=13.5 Hz, H-10), 2.49 (1H, dd, J=13.5, 5.1 Hz, H-10), 2.82 (2H, dd, J=2.6, 2.6 Hz, H-8), 3.16 (1H, dd, J=4.3, 15.5 Hz, H-7), 3.35 (3H, s, Me–O), 3.45 (3H, s, Me–N), 3.61 (3H, s, COOMe), 3.97 (1H, dd, J=5.1, 13.5 Hz, H-10a), 4.75 (1H, dd, J=2.6, 2.6 Hz, H-7), 7.00—7.31 (4H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 29.9, 40.0, 42.8, 43.0, 53.2, 58.2, 58.4, 82.0, 115.0, 123.6, 124.8, 127.3, 128.8, 138.7, 165.3, 170.6, 205.1. MS *m/z*: 317 (M^+). *Anal.* Calcd for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.04; N, 4.41. Found: C, 64.36; H, 6.04; N, 4.30. X-ray analytical data (Fig. 1): $2\theta/\omega$, 3°<2θ <58°, $P2_1/c$, a=7.592 (1), b=27.043 (4), c=7.814 (1) Å, β=105.59 (1)°, V= 1545.2 (3)Å^3, Z=4, D_{calcd}=1.364 g/cm^3, μ (Mo$K\alpha$)=0.94 cm^{-1}. R=0.051 (R_w=0.052).

8a: Colorless columns, mp 202—203 °C (acetone). IR (KBr) cm^{-1}: 1723, 1673, 1603. ^{1}H-NMR ($CDCl_3$) δ: 2.46—2.56 (2H, m, H-10, 10), 2.88—3.10 (2H, m, J=4.6, 14.5 Hz, H-8, 8), 3.34 (3H, s, Me–O), 3.46 (3H, s, Me–N), 3.47 (1H, d, J=7.0, 10.2 Hz, H-10a), 3.59 (3H, s, COOMe), 4.00 (1H, dd, J=4.6, 10.8 Hz, H-7), 7.01—7.14 (3H, m, H-aromatic), 7.27—7.34 (1H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 29.9, 40.0, 42.8, 43.0, 53.2, 58.2, 58.4, 82.2, 115.0, 123.6, 124.8, 127.3, 128.8, 138.7, 165.4, 170.6, 205.1. MS *m/z*: 317 (M^+). *Anal.* Calcd for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.04; N, 4.41. Found: C, 64.54; H, 6.16; N, 4.20.

6b: Colorless columns (acetone–hexane), mp 156—158 °C. IR (KBr) cm^{-1}: 2242, 1670, 1606. ^{1}H-NMR ($CDCl_3$) δ: 2.61—2.82 (2H, m, J=5.0 Hz, H-10, 10), 3.49 (3H, s, Me–N), 3.85 (1H, dd, J=5.0, 12.0 Hz, H-10a), 6.28 (1H, d, J=10.2 Hz, H-8), 7.07 (1H, d, J=10.2 Hz, H-7), 7.13—7.46 (4H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 31.1, 40.0, 41.9, 43.8, 116.1, 116.4, 123.3, 125.0, 127.9, 129.7, 131.5, 137.9, 141.5, 161.1, 193.5. MS *m/z*: 252 (M^+). *Anal.* Calcd $C_{15}H_{12}N_2O_2$: C, 71.41; H, 4.80; N, 11.11. Found: C, 71.18; H, 5.00; N, 10.98.

7b: Colorless columns (acetone–hexane), mp 196—198 °C. IR (KBr) cm^{-1}: 2241, 1725, 1675, 1606. ^{1}H-NMR ($CDCl_3$) δ: 2.20 (1H, dd, J=13.2, 15.2 Hz, H-8), 2.54 (1H, dd, J=5.3, 15.2 Hz, H-8), 2.79 (2H, m, H-10, 10), 3.51 (3H, s, Me–N), 3.54 (3H, s, Me–O), 3.83 (1H, dd, J=5.3, 13.2 Hz, H-10a), 4.59 (1H, dd, J=6.3, 6.3 Hz, H-7), 7.14—7.26 (3H, m, H-aromatic), 7.38—7.44 (1H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 30.8, 39.6, 41.2, 43.3, 47.2, 58.2, 79.1, 116.0, 116.7, 124.7, 125.0, 128.1, 129.5, 137.5, 161.4, 204.0. MS *m/z*: 284 (M^+), 184. *Anal.* Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.34; H, 5.86; N, 9.76.

8b: Colorless columns (acetone–hexane), mp 229—230 °C. IR (KBr) cm^{-1}: 2245, 1726, 1690, 1603. ^{1}H-NMR ($CDCl_3$) δ: 2.86 (2H, d, J=6.6 Hz, H-10, 10), 2.93 (2H, br m, H-8, 8), 3.28 (3H, s, Me–N), 3.48 (3H, s, Me–O), 3.74 (1H, dd, J=6.6, 6.6 Hz, H-10a), 4.13 (1H, dd, J=6.6, 6.6 Hz, H-7), 7.04—7.38 (4H, m, H-aromatic). ^{13}C-NMR ($CDCl_3$) δ: 30.9, 40.0, 40.7, 42.9, 48.4, 59.0, 82.5, 115.1, 117.6, 123.6, 124.4, 126.3, 129.0, 138.5, 162.1, 203.0. MS *m/z*: 284 (M^+), 184. *Anal.* Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.33; H, 5.89; N, 9.83.

9: Yellow columns (acetone–hexane), mp 154 °C. IR (KBr) cm^{-1}: 1651, 1626, 1592. ^{1}H-NMR ($CDCl_3$) δ: 2.69 (1H, dd, J=13.5, 16.5 Hz, H-3′), 3.03 (1H, ddd, J=1.2, 3.5, 16.5 Hz, H-3′), 3.76 (3H, s, Me–N), 5.55 (1H, dd, J=1.2, 6.1 Hz, H-5′), 5.75 (1H, dd, J=3.5, 13.5 Hz, H-2′), 7.29 (1H, ddd, J=1.0, 7.4, 7.4 Hz, H-6), 7.39 (1H, dd, J=1.0, 9.2 Hz, H-8), 7.30 (1H, d, J=6.1 Hz, H-6′), 7.58—7.64 (2H, m, H-5, 7). ^{13}C-NMR ($CDCl_3$) δ: 29.7, 41.4, 76.8, 107.81, 114.2, 119.9, 122.6, 129.2, 129.8, 131.0, 135.1, 139.5, 160.2, 162.8, 191.9. MS *m/z*: 255 (M^+), 227, 198, 184. HR-MS *m/z*: Calcd for $C_{15}H_{13}NO_3$ (M^+): 255.0895. Found: 255.0861. *Anal.* Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.31; H, 5.02; N, 5.31.

10a: Yellow plates (chloroform), mp 297—300 °C. IR (KBr) cm^{-1}: 3607, 1625, 1604. ^{1}H-NMR ($CDCl_3$) δ: 3.89 (3H, s, Me–N), 7.06 (1H, dd, J=2.5, 8.9 Hz, H-8), 7.41 (1H, ddd, J=1.2, 7.1, 8.4 Hz, H-2), 7.51 (1H, dd, J=1.2, 8.6 Hz, H-4), 7.62 (1H, d, J=2.5 Hz, H-10), 7.63 (1H, ddd, J=1.5, 7.1, 8.6 Hz, H-3), 8.15 (1H, dd, J=1.5, 8.4 Hz, H-1), 8.34 (1H, d, J=8.9 Hz, H-7), 9.89 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) δ: 31.2, 106.8, 116.1, 117.6, 119.7, 120.7, 123.6, 124.2, 130.5, 136.6, 136.9, 159.6, 160.1. MS *m/z*: 225 (M^+), 196. HR-MS *m/z*: Calcd for $C_{14}H_{11}NO_2$, 225.0790. Found: 225.0753.

General Procedure for HP-DA Cycloadditions of 1a, b with 2a, b a) A mixture of **1a**, **b** (0.5 mmol) and **2a** (205 mg, 2.5 mmol) in dichloromethane (3 ml) was placed in a Teflon tube, and reacted under conditions

listed in Table 1. The crude products were purified using the same procedure as described above to give **3a**, **b**. b) A mixture of **1a** (108 mg, 0.5 mmol) and **2b** (430 mg, 2.5 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 48 h. The pressure was released and the reaction mixture was purified using the same procedure as described above to give **6a** and **8a**. A mixture of **1b** with **2b** was reacted under conditions listed in Table 2 and the crude products were purified using the same procedure as described above to give **6b**, **7b** and **8b**. The yields of **3a**, **b**, **6a**, **b**, **7a**, **b** and **8a**, **b** are summarized in Tables 1 and 2.

Demethanolation of 7a, b and 8a, b a) The solution of **7a** (25 mg, 0.08 mmol) and 1 ml TFA in 10 ml chloroform was refluxed for 4 h and concentrated *in vacuo.* The residue was purified by preparative TLC over silicagel with ether–isopropyl ether (1 : 3) to give **6a** (22 mg, 97%). The same reaction mixture of **8a** (25 mg, 0.08 mmol) was refluxed for 9 h using the same procedure as described above to give **6a** (22 mg, 97%). b) Demethanolation of **7b** or **8b** (28 mg, 0.08 mmol) was stirred at room temperature for 96 h using the same procedure as described above to give **6b** (20 mg, 79%; 17 mg, 68%), respectively. c) The solution of **7a** (20 mg, 0.064 mmol) in 3 ml *o*-xylene was heated at 180 °C for 3 d and purified using the same procedure as described above to give **6a** (14 mg, 78%).

Calculation of Activation Energy We optimized the structures of the initial and the transition states using the restricted Hartree-Fock (RHF) method at HF/6-31++G (*d*, *p*)//HF/6-31G (*d*) level in the Gaussian 98 program package.[12] 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 a 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 exactly one imaginary vibrational frequency. We also carried out the intrinsic reaction coordinate (IRC) calculation to make sure that the TS connects the initial with the intended final state.

References and Notes

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