Cycloaddition of 2(1*H*)-Pyridones Having a Methoxycarbonyl Group to 1,3-Butadiene Derivatives

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The cycloaddition of 4-methoxycarbonyl-2(1*H*)-pyridones to silyloxydienes gave isoquinolone derivatives in reasonable yields. Furthermore, the cycloaddition of 6-methoxycarbonyl-2(1*H*)-pyridones to 2,3-dimethyl-1,3-butadiene produced cycloadducts (isoquinolone and quinolone derivatives) and double cycloadducts (phenanthridone derivatives). The activation energies using Gaussian 98 with RHF/3-21G level of 4- and 6-methoxycarbonyl-2(1*H*)-pyridones coincided with the experimental facts.

Key words 6-methoxycarbonyl-2(1*H*)-pyridone; phenanthridone; isoquinolone; electron-withdrawing group; cycloaddition; Gaussian 98

2(1*H*)-Pyridones are aromatic heterocyclic compounds and there are many reports on Diels–Alder (DA) reaction of 2(1*H*)-pyridones acting as a diene.[1)] We previously described the novel synthesis of isoquinoline derivatives and isoquinoline alkaloid using the cycloaddition of 2(1*H*)-pyridones having an electron-withdrawing group at the 4-position that acts as a dienophile with alkyl- and alkoxy-1,3-butadienes at atmospheric pressure (AP) (Chart 1).[2,3)] Isoquinolone derivatives having a silyloxy group would be rendered functional by desilylation, but 2(1*H*)-pyridones with useful silyloxydienes have not been cycloadded. On the other hand, 6-acetyl-2(1*H*)-pyridone bearing two dienophilic moieties (Chart 1), and the cycloaddition of 1-substituted and 1-unsubstituted 6-acetyl-2(1*H*)-pyridone to 2,3-dimethyl-1,3-butadiene afforded the phenanthridone derivatives included in some alkaloids,[4)] although at low yield. Although the high pressure strategy can overcome the energy barrier imposed by the steric and electronic effects of cycloaddition,[5)] reactions of 1-substituted and 1-unsubstituted 2(1*H*)-pyridones having an electron-withdrawing group at the 4-position and dienes have not been reported. The present paper describes the cycloaddition of 4- and 6-methoxycarbonyl-1-methyl-2(1*H*)-pyridone to silyloxy- or akyl-1,3-butadienes, at AP and at high pressure (HP), and the reactivity of 4- and 6-methoxycarbonyl-2(1*H*)-pyridones by means of activation energy (E_a) using Gaussian 98[6)] with the RHF/3-21G level.

Cycloaddition Firstly, 4-methoxycarbonyl-1-methyl-2(1*H*)-pyridone (**1**) with 2,3-bis(trimethylsilyloxy)- (**3**) and 2-trimethylsilyloxy-1,3-butadiene (**4**) were cycloadded in a sealed tube under the reaction conditions shown in Table 1. The reaction of **1** with **3** stereoselectively produced the *cis*-isoquinolone adduct [**7** (47%)] having two silyloxy groups and the reaction of **1** with **4** regio- and stereoselectively afforded the fuctionalized *cis*-isoquinolone adduct [**8** (30%)] resulting from desilylation with recovery of **1** (48 %) (Chart 2). Treatment of **7** with weaker acids (10—0.1% HCl) or water provided no desilylated product. The ^{1}H-NMR spectrum and two-dimensional ^{1}H–^{1}H shift correlation spectroscopy of **8** suggested that a ketone occupied the 7-position, since only 2H-8 and H-8a correled. We also examined the HP reactions of **1** and 4-methoxycarbonyl-2(1*H*)-pyridone (**2**) with 2,3-dimethyl- (**5**) and 2,3-dimethoxy-1,3-butadienes (**6**) at HP [10 Kbar, 80—110 °C, 3 d, CH_2Cl_2 (Table 1)]. However, these reactions resulted in diene polymerization and produced *cis*-isoquinolone adducts [**9**[2)] (22%), **10**[3)] (24%), **11**[2)] (none), **12**[3)] (14%)] with recovery of the starting materials.

Next, we cycloadded 6-methoxycarbonyl-1-methyl- (**13**), 6-methoxycarbonyl-2(1*H*)- pyridone (**14**) to **5** at AP [200 °C, 4 d, *o*-xylene (Chart 3)]. This reaction of **13** afforded the *cis*-isoquinolone [**15** (4%)], a new *cis*-quinolone [**16** (5%)], and double cycloaddition adducts [**17** (7%), **18** (10%)]. The reaction of **15** with **5** at HP [10 kbar, 80 °C, 3 d, CH_2Cl_2 (Chart 3)] produced the double cycloaddition adduct (**17**) in 82% yield, whereas the same reaction of **16** did not yield either **17** or **18**. The cycloaddition of **14** afforded the isoquinolone [**19** (4%)] and the double cycloaddition adduct [**20** (18%)]. The methylation of **19** and **20** with methyl iodide (KF-alumina, 2 d, acetonitrile) at room temperature gave the corresponding **15** (90%) and **18** (11%), respectively (Chart 3).

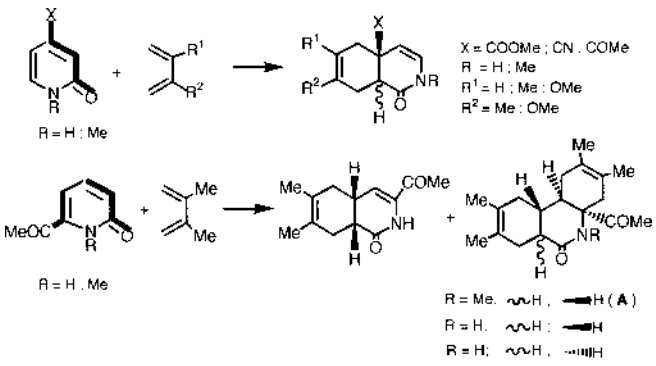

Chart 1

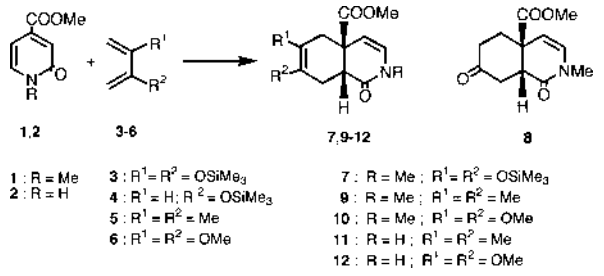

Chart 2

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Table 1. Cycloaddition of **1** and **2** with **3**—**6**

Pyridone	Temp. (°C)	Time (d)	Solvent	Pressure (kbar)	Diene	Adduct	Yield (%)	Recovery of **1** and **2** (%)
1	180	6	Neat	Atmosphere	**3**	**7**	47	38
1	180	3	Neat	Atmosphere	**4**	**8**	30	48
1	80	3	CH_2Cl_2	10	**5**	**9**	22	75
1	110	3	CH_2Cl_2	10	**6**	**10**	24	72
2	110	3	CH_2Cl_2	10	**5**	**11**	0	95
2	110	3	CH_2Cl_2	10	**6**	**12**	14	80

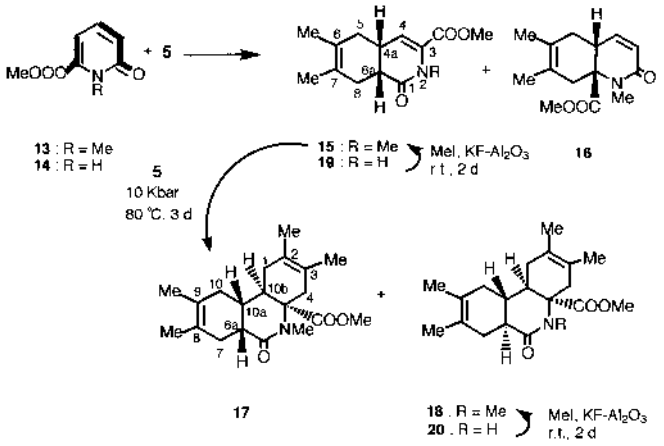


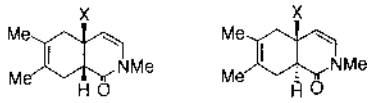
Chart 3

The stereochemistry of the ring junctures in **7**, **8**, and **15**—**20** was confirmed by ^{1}H-NMR spectroscopy and high resolution (HR) MS. Generally, the signals due to H-8a in ^{1}H-NMR spectra of the *cis*-isoquinolone adducts appear at 2.84—2.97 ppm, and those in the *trans*-isoquinolone adducts are located at 2.00—2.80 ppm.[2,3] The corresponding ^{1}H-NMR signals of **7** and **8** appeared at 3.12 and 3.37 ppm, respectively. Therefore, the stereochemistry of the ring junctures in **7** and **8** was confirmed as *cis*. On the other hand, the stereochemistry of the ring junctures in **15**—**20** was determined by comparing the ^{1}H-NMR spectra of **15**—**20** with the *cis-anti-cis*-adduct [A, $J_{6a,10a}$=4.2 Hz, (Chart 1)] confirmed by X-ray[4] and HR-MS spectra analysis. In general, the DA adduct is a *cis* form according to the well-known Alder–Stein rule (*cis* principle) at AP or HP.[5] The stereochemistry of **15** and **19** were deduced as *cis*, based on coupling constants due to H-4a and 8a in the adducts (**15**, J=5.9 Hz; **19**, J=5.5 Hz). Previously, we reported on the MS spectra of *cis*-adducts, and found that large peaks result from the homolytic retro-DA reaction, whereas in the MS spectra of *trans*-adducts, large peaks result from cleavage of carbon–carbon bonds (Table 2).[7] The double cycloaddition adducts (**17**, **18**) having the same molecular formula based on HR-MS were stereoisomers. The HR-MS spectrum of **17** showed a base ion peak at *m/z* 167 [M−two diene]$^+$ resulting from the double retro-DA reaction. The HR-MS spectrum of **18** revealed a predominate ion peak at *m/z* 249 [M−diene]$^+$ resulting from the retro-DA reaction. These findings confirmed that the stereochemistry of the two ring junctures in **17** was *cis*, and that of the ring junctures in **18** consisted of *cis* and *trans*. The *cis-anti-cis*-adduct (**17**) may have been isomerized by heating to give *cis-anti-trans*-adduct (**18**) during the reaction. The stereochemistry between protons at 10a and 10b in **17** was deduced as follows. If the stereochemistry between protons at 10a and 10b in **17** was the *syn*-form, **17** would show steric interactions between protons at 1 and 10, and the ester and *N*-methyl groups, whereas if it was the *anti*-form, **17** would be released from these interactions as shown by X-ray analysis of **A**.[4] Further, in the ^{1}H-NMR spectra of **17**, the coupling constant (J=7.0 Hz) due to H-10a and 10b (axial and axial) suggested the *anti*-form. Based on the above considerations, the stereochemistry between H-10a and 10b in **17** was deduced to be the *anti*-form. Similarly, that in **18** was deduced to be the *anti*-form. The stereochemistry in **20** was *cis-anti-trans*, since methylation of **20** gave **18**. The structure of the adduct (**16**) was confirmed as follows. The adducts (**15**, **16**) have the same molecular formulae based on the HR-MS spectra. The ^{1}H-NMR spectrum of **16** showed signals due to H-3 and 4 at 5.87 ppm (J=9.9 Hz) and 6.65 ppm (J=9.9 Hz), respectively. These results indicated that the adduct (**16**) was the quinolone derivative. The stereochemistry of ring juncture in **16** was confirmed as *cis*, since the HR-MS spectrum of **16** showed an ion peak at *m/z* 167 [M−diene]$^+$ resulting from the retro-DA reaction (Table 2).

We theoretically determined whether the 3,4- or 5,6-addition occurs in the DA reactions listed in Table 3. We searched and optimized the structures of the transition states (TS) using Gaussian 98[6] with RHF/3-21G level. We assumed that the diene and dienophile were far apart in the initial state, and regarded the difference in energy between TS and the initial state as the activation energy (E_a). The optimized structures of TS in the DA reactions of **5** with **13** are shown in Fig. 1. In Fig. 1, we also show the bond orders of the TS calculated using AM1 method[8] with the optimized structures. Table 3 summarizes the calculated activation energies of these four reactions together with the experimental yields of the adducts. During the DA reactions of **3**, **4**, and **5** with **1**, the E_a for the 3,4-addition was much smaller than that for the 5,6-addition. On the other hand, during the DA reaction of **5** with **13**, the E_a for the 3,4-addition has a value of 35.77 kcal/mol, which is only 1.29 kcal/mol smaller than that for the 5,6-addition and considerably larger than that for the 3,4-addition in the other DA reactions in Table 3. These results are consistent with the experimental finding that only adducts from the 3,4-addition were obtained in the DA reaction of **3**, **4**, and **5** with **1**. However, both types of adducts were experimentally obtained but in rather small yields in the DA reaction of **5** with **13**.

In conclusion, the cycloaddition of 4-methoxycarbonyl-2(1*H*)-pyridones to silyloxydienes stereo- and regioselectively afforded the isoquinolone derivatives in reasonable yields. In contrast, cycloaddition at HP did not yield satisfac-

Table 2. MS of *cis*- and *trans*-Adducts



21[7]: X = CN
22[7]: X = COOMe
23[7]: X = CN
24[7]: X = COOMe

Adduct	MS *m/z*				
	M^+	M^+-diene	M^+-2diene	Diene$^+$	M^+-R
15	249	167		82	
16	249	167		82	
17	331		167	82	
18	331	249		82	190 (249−COOMe)
21	216	134		82	
22	249	167		82	
23	216				173 (M−CO−Me)
24	249				190 (M−COOMe)

Table 3. Experimental Yields of Adducts and Calculated Activation Energies for the DA Reactions of **1** and **13** with **3**, **4**, and **5**

Diene	Dienophile	3,4-Addition		5,6-Addition		ΔE_a[a] (kcal/mol)
		E_a (kcal/mol)	Yields (%)	E_a (kcal/mol)	Yields (%)	
3	**1**	33.48	47	39.77		6.29
4	**1**	31.77	30	38.01		6.24
5	**1**	32.49	85[b]	40.46		7.97
5	**13**	35.77	2[c]	37.06	5	1.29

a) Difference in activation energy (E_a) between 5,6-addition and 3,4-addition. *b*) Ref. 2*a*, *b*). *c*) Sum of the yields of **15**, **17**, and **18**.

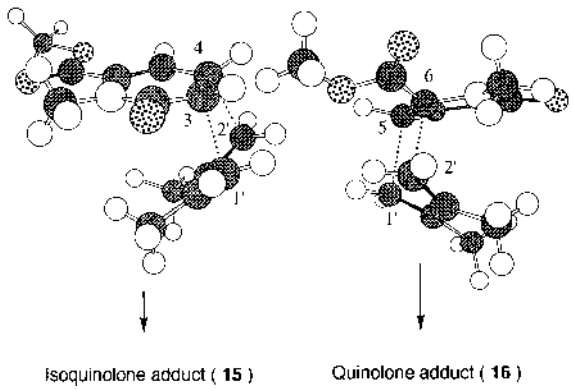


Fig. 1. Calculated Structures of TS for 3,4-Addition (Left) and for 5,6-Addition (Right) in the DA Reactions of **5** with **13**

The calculated relevant interatomic distances are: C_3C_4=1.395 Å, $C_3C_{1'}$=2.110 Å, $C_4C_{2'}$=2.227 Å (left); C_5C_6=1.411 Å, $C_5C_{1'}$=2.095 Å, $C_6C_{2'}$=2.269 Å (right). The corresponding bond orders calculated using AM1 method[8] with above structures are: C_3C_4=1.448, $C_3C_{1'}$=0.314, $C_4C_{2'}$=0.259 (left); C_5C_6=1.367, $C_5C_{1'}$=0.331, $C_6C_{2'}$=0.248 (right).

tory results. Furthermore, the cycloaddition of 6-methoxycarbonyl-2(1*H*)-pyridones with alkyldiene afforded cycloaddition adducts (isoquinolone and new quinolone derivatives) and double cycloaddition adducts (phenanthridone derivatives). The activation energies (E_a) determined using Gaussian 98[6] with RHF/3-21G level of 4- and 6-methoxycarbonyl-2(1*H*)-pyridones coincided with the experimental facts.

Experimental

Melting points were determined on a Yanaco melting point apparatus and are uncorrected. IR spectra were measured with a Perkin Elmer FT-IR 1725X spectrophotometer. MS and HR-MS were performed using a JEOL JMS-DX303/JMA-DA5000 spectrometer. ^{1}H-NMR spectra were recorded on JNM-GSX400, JNM-EX270, and JEOL-JNM-PMX60 spectrometers with tetramethylsilane (TMS) as the internal standard. The coupling patterns are indicated as follows: s, singlet; d, doublet; dd, double doublet; ddd, double double doublet; m, multiplet; br, broad. Preparative TLC was proceeded on precoated Silica gel 60F_{254} TLC plate (2 mm), Merck. Chromatography was performed on Merck Kieselgel 60 (230—400 mesh).

General Procedure for Cycloaddition of 1 or 2 with 3 or 4 A mixture of **1** (835 mg, 5 mmol) and **3** (2.40 g, 7.5 mmol) was heated in a sealed tube under the conditions as shown in Table 1. The reaction mixture was separated by chromatography on a column of silica gel. The residue of the first fraction eluted with acetone was purified by preparative TLC over silica gel with ether–hexane (1 : 1) to give *cis*-1,2,4a,5,8,8a-hexahydro-4a-methoxycarbonyl-2-methyl-6,7-bis(trimethylsilyloxy)-isoquinolin-1-one (**7**). The solvent of the second fractions eluted with acetone were evaporated to recover **1** [317 mg, (38%)]. The reaction of **1** (835 mg, 5 mmol) with **4** (1.73 g, 7.5 mmol) proceeded in a similar manner to that described above to give 1,2,4a,5,6,7,8,8a-octahydro-4a-methoxycarbonyl-2-methyl-isoquinolin-1,7-dione (**8**) with recovery of the starting material [**1**, 400 mg (48%)]. The yields of **7** and **8** are listed in Table 1.

7: Pale brown oil. IR (film) cm^{-1}: 1737, 1682, 1132, 1082. ^{1}H-NMR ($CDCl_3$) δ: 0.15 (9H, s), 0.17 (9H, s), 2.21—2.77 (4H, m), 3.06 (3H, s), 3.12 (1H, m), 3.72 (3H, s), 5.05 (1H, d, J=7.7 Hz), 6.06 (1H, d, J=7.7 Hz). ^{13}C-NMR ($CDCl_3$) δ: 0.74, 0.78, 26.79, 34.09, 34.93, 41.73, 45.86, 52.54, 108.80, 128.21, 130.58, 130.83, 169.62, 173.39. MS *m/z* : 397 (M^+), 240, 168. HR-MS *m/z*: 397.1742 (Calcd for $C_{18}H_{31}NO_5Si_2$: 397.1741).

8: Pale brown oil. IR (film) cm^{-1}: 1726, 1682. ^{1}H-NMR ($CDCl_3$) δ: 2.17—2.49 (4H, m), 2.56 (1H, ddd, J=1.3, 6.9, 14.0 Hz), 2.85 (1H, ddd, J=1.3, 6.9, 14.0 Hz), 3.08 (3H, s), 3.37 (1H, ddd, J=0.7, 6.9, 6.9 Hz), 3.77 (3H, s), 5.08 (1H, dd, J=0.7, 7.8 Hz), 6.18 (1H, d, J=7.8 Hz). ^{13}C-NMR

($CDCl_3$) δ: 31.21, 34.11, 37.44, 38.42, 44.66, 45.96, 52.89, 106.37, 131.91, 168.38, 173.07, 206.62. MS *m/z*: 237 (M^+), 178. HR-MS *m/z*: 237.0978 (Calcd for $C_{12}H_{15}NO_4$: 237.1001).

General Procedure for HP Cycloaddition of 1 or 2 to 5 or 6 A mixture of **1** or **2** (1.5 mmol) and **5** or **6** (5 mmol) was heated in a Teflon tube under the conditions shown in Table 1. The reaction mixture was chromatographed on a column of silica gel. This procedure was repeated using the residue of the first fraction eluted with acetone. The first fraction eluted benzene–acetone (10 : 1) gave **9**,[2] **10**,[3] **12**,[3] respectively. The yields of **9**—**12** are listed in Table 1.

Cycloaddition of 13 with 5 A solution of **13** (0.50 g, 3 mmol) and **5** (1.25 g, 15 mmol) in *o*-xylene 2 ml was heated at 200 °C for 4 d in a sealed tube. The solvent was evaporated and the residue was purified by preparative TLC over silica gel with ether to give *cis*-1,2,4a,5,8,8a-hexahydro-3-methoxycarbonyl-2,6,7-trimethylisoquinolone [**15**, *Rf*=0.67, 32 mg (4%)] and *cis-anti-trans*-1,4,4a,5,6,6a,7,10,10a,10b-decahydro-4a-methoxy-carbonyl-2,3,5,8,9-pentamethylphenanthridin-6-one [**18**, *Rf*=0.55, 98 mg (10%)], and **13** [*Rf*=0.19, 0.35 g (70%)]. The mixture (*Rf*=0.38) of *cis*-1,2,4a,5,8,8a-hexahydro-8a-methoxycarbonyl-1,6,7-trimethylquinolin-1-one (**16**) and *cis-anti-cis*-1,4,4a,5,6,6a,7,10, 10a,10b-decahydro-4a-methoxycarbonyl-2,3,5,8,9-hexamethylphenanthridin-6-one (**17**) was purified by distillation to give **16** [40 mg (5%)] and **17** [14 mg (7%)].

15: Pale yellow oil. IR (film) cm^{-1}: 1728, 1682. ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3H, s), 1.63 (3H, s), 1.87 (1H, d, *J*=17.2 Hz), 2.00—2.16 (2H, m), 2.41 (1H, d, *J*=18.3 Hz), 2.63 (1H, m, *J*=5.9, 11.7 Hz), 2.75 (1H, ddd, *J*=5.1, 5.9, 12.2 Hz), 3.15 (3H, s), 3.81 (3H, s), 6.33 (1H, d, *J*=4.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 18.89, 19.13, 29.15, 30.18, 31.86, 32.93, 38.70, 52.28, 122.97, 124.92, 125.74, 133.94, 163.16, 172.74. MS *m/z*: 249 (M^+), 167 ($M^+-C_6H_{10}$). HR-MS *m/z*: 249.1369 (Calcd for $C_{14}H_{19}NO_3$: 249.1365).

16: Colorless crystalline powder (ether). mp 62—65 °C. IR (KBr) cm^{-1}: 1739, 1652. ^{1}H-NMR ($CDCl_3$) δ: 1.62 (3H, s), 1.66 (3H, s), 1.89 (1H, m), 2.19 (1H, m), 2.40 (1H, m), 2.63 (1H, m), 2.95 (3H, s), 3.02 (1H, m), 3.70 (3H, s), 5.87 (1H, d, *J*=9.9 Hz), 6.65 (1H, dd, *J*=5.9, 9.9 Hz). ^{13}C-NMR ($CDCl_3$) δ: 18.24, 18.54, 27.98, 35.26, 36.23, 36.88, 52.77, 65.76, 120.54, 124.65, 126.20, 143.95, 165.67, 174.74. MS *m/z*: 249 (M^+), 167 ($M^+-C_6H_{10}$), 108. HR-MS *m/z*: 249.1347 (Calcd for $C_{14}H_{19}NO_3$: 249.1365).

17: Colorless columns (ether–hexane). mp 153—156 °C. IR (KBr) cm^{-1}: 1736, 1652. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (12H, s), 1.85 (1H, d, *J*=16.1 Hz), 1.93 (2H, s), 2.03 (1H, d, *J*=17.2 Hz), 2.12 (3H, m, *J*=3.7, 7.0, 11.7 Hz), 2.34—2.45 (2H, m, *J*=3.7, 4.2, 7.0, 10.0, 10.0 Hz), 2.70 (1H, ddd, *J*=4.2, 7.5, 11.5 Hz), 2.75 (3H, s), 2.88 (1H, d, *J*=17.2 Hz), 3.75 (3H, s). ^{13}C-NMR ($CDCl_3$) δ: 18.43, 18.61, 18.91, 19.16, 29.52, 30.77, 31.50, 32.38, 33.26, 37.27, 40.77, 52.80, 68.13, 121.48, 122.56, 122.71, 123.68, 173.15, 173.16. MS *m/z*: 331 (M^+), 167 ($M^+-2C_6H_{10}$), 82. HR-MS *m/z*: 331.2151 (Calcd for $C_{20}H_{29}NO_3$: 331.2147).

18: Colorless crystalline powder (ether–hexane). mp 161—164 °C. IR (KBr) cm^{-1}: 1737.5, 1648. ^{1}H-NMR ($CDCl_3$) δ: 1.62 (6H, s), 1.65 (6H, s), 1.72—1.77 (2H, m, *J*=4.2, 7.0, 9.5 Hz), 1.96—2.01 (4H, m), 2.09 (1H, d, *J*=17.2 Hz), 2.16—2.20 (2H, m, *J*=3.7, 4.7, 6.2 Hz), 2.56 (1H, d, *J*=16.9 Hz), 2.78 (3H, s), 2.88 (1H, d, *J*=17.6 Hz), 3.76 (3H, s). ^{13}C-NMR ($CDCl_3$) δ: 18.46, 18.78, 18.82, 18.89, 30.54, 30.67, 33.67, 34.44, 33.26, 36.89, 37.80, 40.38, 43.75, 52.74, 67.55, 121.60, 122.47, 124.05, 126.10, 171.47, 172.77. MS *m/z*: 331 (M^+), 249 ($M^+-C_6H_{10}$), 190. HR-MS *m/z*: 331.2127 (Calcd $C_{20}H_{29}NO_3$: 331.2147).

Cycloaddition of 14 with 5 A solution of **14** (0.765 g, 5 mmol) and **5** (2.05 g, 25 mmol) in *o*-xylene (2 ml) was heated at 200 °C for 4 d in a sealed tube. The reaction mixture was chromatographed on a column of silica gel. The residue of the first fraction eluted with acetone was purified by a preparative TLC over silica gel with ether–hexane (1 : 1) to give *cis*-1,2,4a,5,8,8a-hexahydro-3-methoxycarbonyl-6,7-dimethylisoquinolin-1-one [**19**, *Rf*=0.51, 54 mg (4%)]. The residue of the second fraction eluted with acetone gave *cis-anti-trans*-1,4,4a,5,6,6a,7,10,10a,10b-decahydro-4a-methoxycarbonyl-2,3,8,9-tetramethylphenanthridin-6-one [**20**, 0.288 g, (18%)], and that of the second fraction recovered **14** (0.16 g, 21%).

19: Colorless needles (ether). mp 96—99 °C. IR (KBr) cm^{-1}: 3243, 3134, 1727, 1676. ^{1}H-NMR ($CDCl_3$) δ: 1.60 (3H, s), 1.64 (3H, s), 1.95 (1H, m), 2.10 (2H, m), 2.48 (1H, d, *J*=16.9 Hz), 2.66 (1H, dd, *J*=5.5, 12.1 Hz,), 2.84 (1H, ddd, *J*=1.8, 5.5, 12.1 Hz), 3.83 (3H, s), 6.27 (1H, d, *J*=5.1 Hz), 7.26 (1H, br s). ^{13}C-NMR ($CDCl_3$) δ: 18.87, 19.08, 28.71, 31.25, 32.89, 38.47, 52.60, 120.31, 123.35, 124.61, 127.82, 162.28, 171.94. MS *m/z*: 235 (M^+), 153 ($M^+-C_6H_{10}$), 95. HR-MS *m/z*: 235.1239 (Calcd for $C_{13}H_{17}NO_3$: 235.1208).

20: Colorless needles (ether). mp 181—184 °C. IR (KBr) cm^{-1}: 3178, 3068, 1742, 1662. ^{1}H-NMR ($CDCl_3$) δ: 1.57 (3H, s), 1.60 (3H, s), 1.63 (6H, m), 1.70—1.83 (2H, m), 2.02—2.16 (4H, m), 2.19—2.23 (2H, m), 2.37 (1H, d, *J*=17.6 Hz), 2.48 (1H, d, *J*=17.6 Hz), 2.58 (1H, d, *J*=17.2 Hz), 3.73 (3H, s), 6.02 (1H, br s). ^{13}C-NMR ($CDCl_3$) δ: 18.48, 18.67, 18.70, 18.86, 31.22, 33.35, 34.64, 37.09, 38.35, 41.15, 42.79, 52.77, 61.37, 121.09, 123.80, 124.37, 125.57, 172.55, 173.07. MS *m/z*: 317 (M^+), 235 ($M^+-C_6H_{10}$), 176. HR-MS *m/z*: 317.1994 (Calcd for $C_{19}H_{27}NO_3$: 317.1991).

Cycloaddition of 15 with 5 A solution of **15** (60 mg, 0.241 mmol) and **5** (0.198 g, 2.41 mmol) in CH_2Cl_2 1 ml was heated under 10 kbar at 80 °C, 3 d in a Teflon tube. The solvent was evaporated and the residue was purified by a preparative TLC over silica gel with ether to give **17** [*Rf*=0.46, 65 mg (82%)].

Methylations of 19 and 20 MeI (0.03 ml, 0.414 mmol) was added to a suspension of acetonitrile (6 ml), **19** (65 mg, 0.27 mmol), and KF-Al_2O_3 (40 mg, 0.69 mmol) under a nitrogen atmosphere. The suspension was stirred at room temperature for 2 d. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was purified by preparative TLC over silica gel with ether–hexane to give **15** (*Rf*=0.29, 62 mg, 90%). Methylation of **20** [80 mg, 0.257 mmol, KF-Al_2O_3 (37 mg, 0.63 mmol), MeI (0.025 ml, 0.378 mmol)] was worked up in a similar manner as described above. The residue was purified by preparative TLC over silica gel with ether to give **18** (*Rf*=0.41, 9 mg, 11%) with recovery of **20** (*Rf*=0.30, 44 mg, 54%).

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