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Studies on Ketene and Its Derivatives. CXVI.[1] Some Reactions of 3-Oxocyclobuta[*c*]quinoline-2-spiro-2′-oxetane —[4+2] Cycloaddition *via ortho*-Azaquinodimethane—

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2-Methylenehexahydrocyclobuta[*c*]quinoline **2** obtained from cyclobuta[*c*]quinolinespirooxetanone **1** was isomerized to 2-methyltetrahydrocyclobuta[*c*]quinoline **5** by treatment with sodium ethoxide in dry toluene. The reaction of compound **5** with olefins, such as methyl acrylate, acrylonitrile, *N*-phenylmaleimide, and methyl methacrylate under reflux in dry xylene gave [4+2] cycloadducts, hexahydrophenanthridine derivatives **6**—**9**. Ethoxycarbonylmethylcyclobuta[*c*]quinolines **4** generated by ethanolysis of **1** were treated with thionyl chloride in pyridine to give dehydrated products, (*E*)-2-(ethoxycarbonylmethylene)cyclobuta[*c*]quinoline (*E*)-**13** and its isomer (*Z*)-**13**. Compounds (*E*)-**13** and (*Z*)-**13** isomerized to the same product, 2-(ethoxycarbonylmethyl)cyclobuta[*c*]quinoline **14** in the presence of sodium ethoxide in dry benzene at room temperature. Similarly, compound **14** reacted with olefins to give hexahydrophenanthridine derivatives **15**—**18** *via* a 2-oxoquinoline-3,4-diquinomethane intermediate.

Keywords——tetrahydrocyclobuta[*c*]quinoline; 2-oxoquinoline-3,4-diquinomethane; isomerization; (*E*),(*Z*)-isomer; [4+2] cycloaddition; hexahydrophenanthridine derivative

Previously, we reported that the photoreaction of diketene with 2-quinolone gave a [2+2] cycloadduct, cyclobuta[*c*]quinolinespirooxetanone **1**, which was transformed either to 2-methylenecyclobuta[*c*]quinoline **2** by thermolysis or to methoxycarbonylmethylcyclobuta[*c*]quinoline **3** by treatment with methanol saturated with dry hydrogen chloride.[2] Recently, Kaneko *et al.*[3,4] reported that the cyclobuta[*c*]quinoline obtained from the photoreaction of 2-quinolone and olefin gave a [4+2] cycloadduct *via* a 2-oxoquinoline-3,4-diquinomethane intermediate on heating.

In the present paper we wish to report [4+2] cycloaddition *via* an azaquinodimethane species generated from cyclobuta[*c*]quinoline obtained by the isomerization of compounds **2** and **13**.

Compound **2** was treated with sodium ethoxide in dry toluene to give 2,4-dimethyl-3-oxo-1,2,3,4-tetrahydrocyclobuta[*c*]quinoline (**5**) in 57% yield. Structural assignment was achieved as follows; elemental analysis showed the same empirical formula ($C_{13}H_{13}NO$) as that of the starting material **2**. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed signals due to the C_2-methyl protons as a doublet and the C_1-methylene protons as two double-doublets. These data are consistent with the 2,4-dimethyl-3-oxo-1,2,3,4-tetrahydrocyclobuta[*c*]quinoline structure **5**.

It was reported that heating of tetrahydrocyclobuta[*c*]quinoline resulted in the formation of the azaquinodimethane intermediate, which reacted with olefins to yield [4+2] cycloadducts, hexahydrophenanthridines.[3,4] We investigated the reaction of compound **5** with olefins under heating. Namely, heating of **5** with methyl acrylate in dry xylene gave 8-methoxycarbonyl-5,7-dimethyl-6-oxo-5,6,7,8,9,10-hexahydrophenanthridine (**6**) in 73% yield.

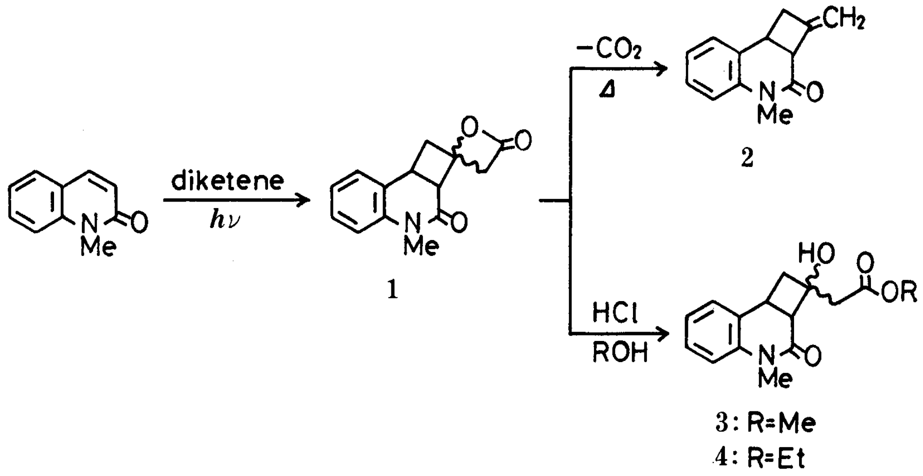


Chart 1

Similarly, reaction of compound **5** with acrylonitrile and *N*-phenylmaleimide afforded the corresponding hexahydrophenanthridine derivatives **7** and **8** in 54 and 80% yields, respectively. Heating of **5** and methyl methacrylate gave an inseparable mixture (*trans*-**9** and *cis*-**9** in *ca*. 2:1 ratio) in 78% yield.

Oxidation of compound **6** was carried out in the expectation of proving that olefins added regiospecifically to **5**. Thus, compound **6** was oxidized with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in dry benzene to give 8-methoxycarbonyl-5,7-dimethyl-6-oxo-5,6-dihydrophenanthridine (**10**) in 24% yield. The ^{1}H-NMR spectrum showed signals due to aromatic protons of C_9 and C_{10} as dobulets ($J=8$ Hz) at 7.08 and 8.43 ppm, respectively. Since the chemical shifts of C-ring protons of compounds **7** and **9** were similar to that of compound **6**, we assigned 8-substituted structures to the products, **7** and **9**.

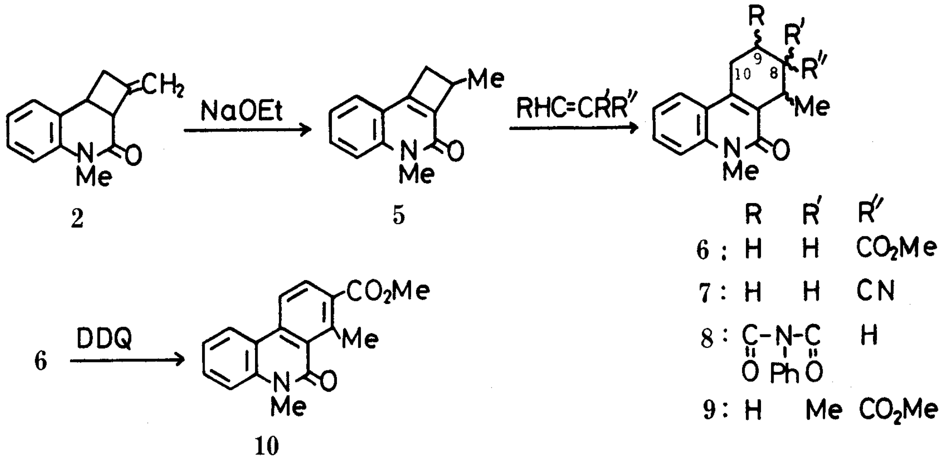


Chart 2

We next investigated the allylic alkylation of compound **2** under the palladium-catalyzed conditions reported by Trost.[5,6] Treatment of compound **2** with sodium palladium chloride in acetic acid gave the π-allyl palladium complex **11** in 55% yield. Reaction of diethyl malonate with this complex yielded 2-(2,2-bis(ethoxycarbonyl)ethyl)-4-methyl-3-oxo-2a,3,4,8b-tetrahydrocyclobuta[*c*]quinoline (**12**) in 55% yield. Elemental analyses and spectroscopic data were consistent with the assigned structures, as detailed in the experimental section.

Compound **12** did not isomerize to 1,2,3,4-tetrahydrocyclobuta[*c*]quinoline in the manner described for compound **5**.

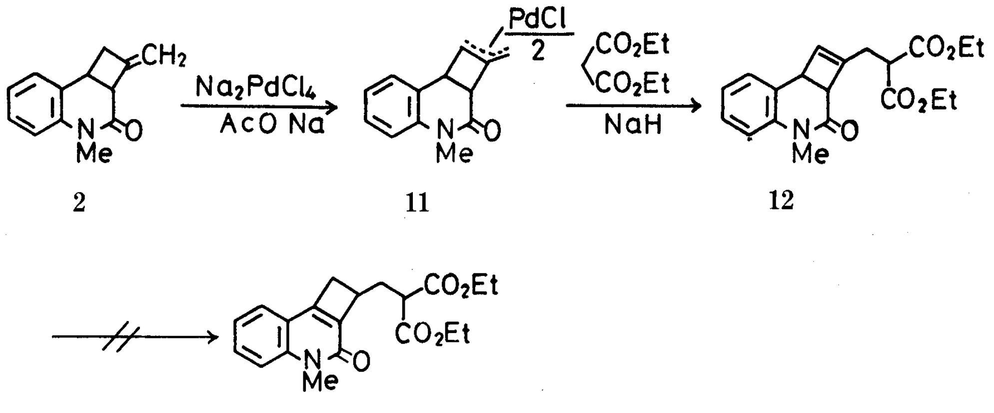


Chart 3

Next, attempts were made to prepare the tetrahydrocyclobuta[*c*]quinoline from compound **4**.[7] Treatment of *cis*-**4** with thionyl chloride in pyridine gave the dehydrated products, (*E*)-2-(ethoxycarbonylmethylene)-4-methyl-3-oxo-1,2,2a,3,4-8b-hexahydrocyclobuta[*c*]-quinoline ((*E*)-**13**) and the (*Z*)-isomer ((*Z*)-**13**) in 66 and 4% yields, respectively. Similarly, dehydration of *trans*-**4** yielded (*E*)-**13** and (*Z*)-**13** in 50 and 9% yields, respectively. Structural assignments of these products were made on the basis of elemental analyses and spectroscopic data. Specifically, the infrared (IR) spectra of products (*E*)-**13** and (*Z*)-**13** showed the absence of the hydroxyl group, and the ^{1}H-NMR spectra showed signals of the C_{2a} methine proton of compound (*Z*)-**13** at lower field (4.85—5.13 ppm) than those of compound (*E*)-**13** (3.17—4.36 ppm).

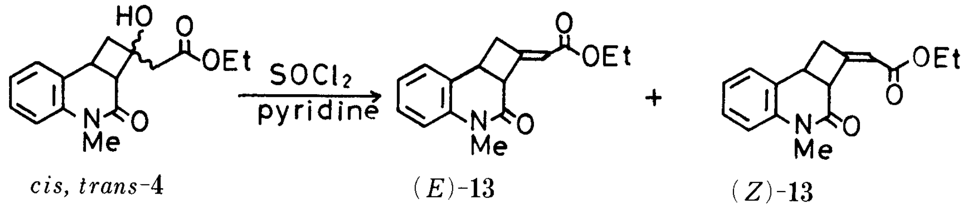
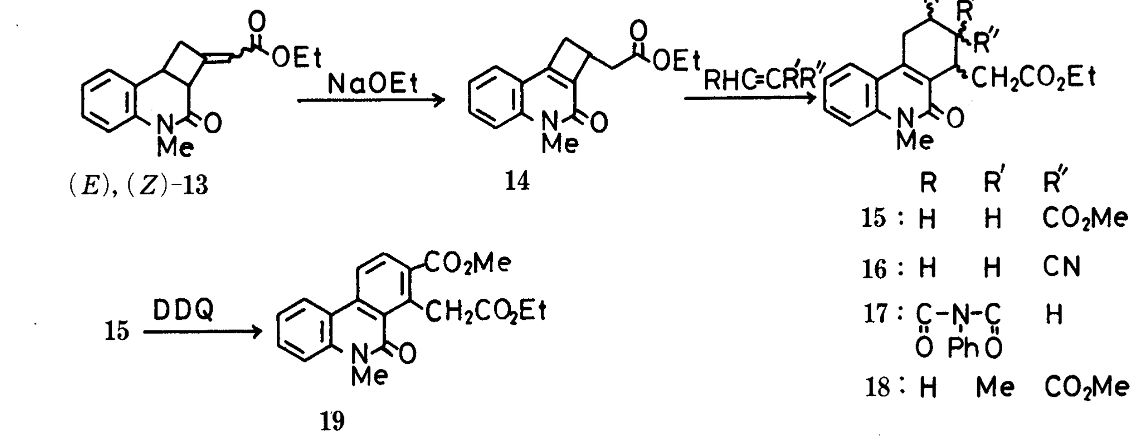


Chart 4

Compound (*E*)-**13** (or (*Z*)-**13**) was treated with sodium ethoxide in dry benzene at room temperature to give 2-(ethoxycarbonylmethyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclobuta[*c*]quinoline (**14**) in 40% yield. Compound **14** reacted with olefins to yield hexahydrophenanthridine derivatives. Namely, heating of compound **14** with methyl acrylate in dry xylene gave 7-(ethoxycarbonylmethyl)-8-methoxycarbonyl-5-methyl-6-oxo-5,6,7,8,9,10-hexahydrophenanthridine (**15**) in 90% yield. Similarly, compound **14** reacted with acrylonitrile and *N*-phenylmaleimide to afford **16** and **17** in 70 and 90% yields, respectively. Reaction of compound **14** with methyl methacrylate also gave a mixture of *cis*- and *trans*-**18** in 87% yield (ratio of *cis*: *trans*, *ca.* 1 : 4).

Oxidation of compound **15** with DDQ furnished 7-(ethoxycarbonylmethyl)-8-methoxycarbonyl-5-methyl-6-oxo-5,6-dihydrophenanthridine (**19**) in 19% yield. Elemental analyses and spectroscopic data for compounds **14**—**19** were consistent with the assigned structures, as detailed in the experimental section.

These experiments revealed that tetrahydrocyclobuta[*c*]quinolines **5** and **14** can serve as *ortho*-azaquinodimethanes in [4+2] cycloaddition. The cycloaddition of compounds **5** and **14** to olefin showed regioselectivity. Although the details of the mechanism of the regioselective cycloaddition of compounds **5** and **14** are not clear at present, Kaneko *et al.*[4]



	R	R'	R''
15 :	H	H	CO_2Me
16 :	H	H	CN
17 :	$\overset{O}{\underset{\|}{C}}$-N(Ph)-$\overset{O}{\underset{\|}{C}}$		H
18 :	H	Me	CO_2Me

Chart 5

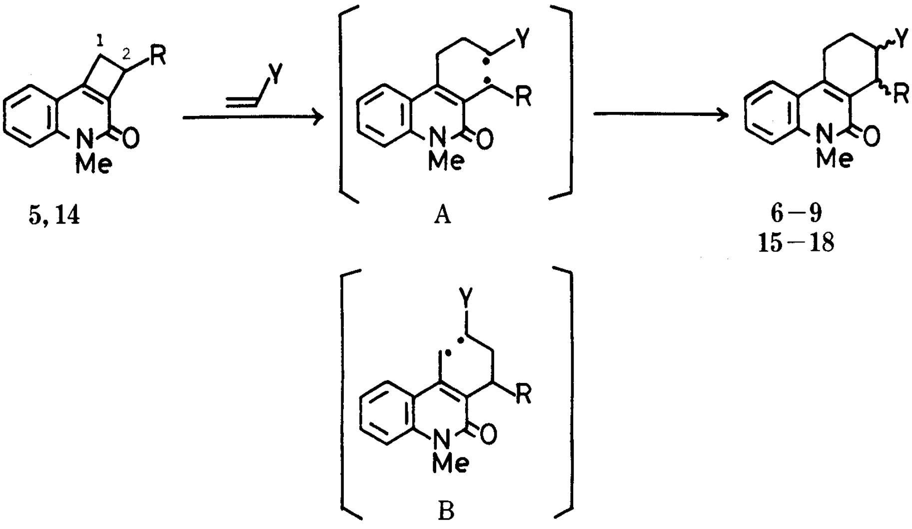


Chart 6

suggested that the stability of the biradical intermediates **A** and **B** is affected by the substituent on the cyclobutene ring. A likely pathway is as follows: a 2-alkyl substituent preferentially stabilizes a biradical intermediate **A**, which gives a cycloadduct.

Experimental

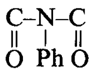
Melting points are uncorrected. IR spectra were taken on a JASCO IR-S spectrometer. ^{1}H-NMR spectra were recorded on JEOL PS 100 (for **9** and **18**) and JEOL JMN-PMX 60 instruments using tetramethylsilane as an internal standard.

2,4-Dimethyl-3-oxo-1,2,3,4-tetrahydrocyclobuta[*c*]quinoline (5)——A mixture of 4-methyl-2-methylene-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline (**2**)[2] (4.98 g, 0.025 mol) and sodium ethoxide (1.7 g, 0.025 mol) in toluene (40 ml) was refluxed for 7 h. The reaction mixture was concentrated under reduced pressure. The resulting residue was poured into water and the mixture was extracted with chloroform. The chloroform layer was dried over sodium sulfate and concentrated. The residue was chromatographed on a silica gel column. Elution with chloroform gave a crystalline product, which was recrystallized from hexane to give the product **5** as needles (2.86 g, 57%), mp 98.5—99.5 °C. *Anal.* Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.57; H, 6.64; N, 7.08. IR ($CHCl_3$): 1660, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.47 (3H, d, $J=7$ Hz, C_2-CH_3), 2.64 (1H, dd, $J=14$ Hz, $J=1$ Hz, C_1-Ha), 3.35 (1H, dd, $J=14$ Hz, $J=4$ Hz, C_1-Hb), 3.43—3.63 (1H, m, C_2-H), 3.77 (3H, s, NCH_3), 7.00—7.53 (4H, m, aromatic protons).

Reaction of Compound 5 with Olefins: General Procedure——A solution of **5** (597 mg, 3 mmol) and olefin (90 mmol) in xylene (100 ml) was refluxed. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography to give 7-methyl-5,6,7,8,9,10-hexahydrophenanthridines **6**—**9**. The results are listed in Tables I and II.

8-Methoxycarbonyl-5,7-dimethyl-6-oxo-5,6-dihydrophenanthridine (10)——A solution of **6** (285 mg, 1 mmol) and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (454 mg, 2 mmol) in dry benzene (10 ml) was refluxed for 20 h. The precipitates were filtered off and the filtrate was concentrated *in vacuo*. The resulting residue was chromatographed over silica gel. Elution with hexane–ethyl acetate (10 : 1) gave a crystalline product, which was recrystallized from hexane to give the product **10** as prisms (68 mg, 24%), mp 135—136 °C. *Anal.* Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.34; H, 5.34; N, 4.89. IR ($CHCl_3$): 1720, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.93 (3H, s, C_7-

TABLE I

Product				Reaction time (h)	Eluent in silica gel column chromatography	Solvent for recrystallization	mp (°C)	Yield (%)
No.	R	R′	R″					
6	H	H	CO_2Me	15	Benzene–ethyl acetate (10 : 1)	Petroleum ether	124—126	73
7	H	H	CN	15	Benzene–ethyl acetate (10 : 1)	Benzene–hexane	167—168	54
8	 $\underset{\underset{\displaystyle O}{\Vert}}{C}-\underset{\underset{\displaystyle Ph}{\vert}}{N}-\underset{\underset{\displaystyle O}{\Vert}}{C}$		H	10	—	Benzene	248—250 (dec.)	80
9	H	Me	CO_2Me	15	Chloroform	Petroleum ether	95—100	78[a]

[a] Mixture of *cis* and *trans*.

TABLE II

Product No.	Formula	Analysis (%) Calcd (Found)			IR ($CHCl_3$) cm^{-1}	NMR ($CDCl_3$) δ
		C	H	N		
6	$C_{17}H_{19}NO_3$	71.56 (71.28	6.71 6.62	4.91 4.84)	1720, 1630	1.21 (3H, d, J=7 Hz, C_7-Me), 1.93—2.33 (2H, m, C_9-H), 2.40—3.10 (3H, m, C_8-H and C_{10}-H), 3.50—3.64 (1H, m, C_7-H), 3.74 (3H, s, NMe), 3.76 (3H, s, OMe), 7.03—7.84 (4H, m, Ar-H)
7	$C_{16}H_{16}N_2O$	76.16 (76.32	6.39 6.39	11.10 11.05)	2250, 1630	1.41 (3H, d, J=7 Hz, C_7-Me), 1.97—2.33 (2H, m, C_9-H), 2.77—3.21 (3H, m, C_8-H and C_{10}-H), 3.46—3.68 (1H, m, C_7-H), 3.74 (3H, s, NMe), 7.10—7.77 (4H, m, Ar-H)
8	$C_{23}H_{20}N_2O_3$	74.17 (74.44	5.41 5.55	7.52 7.23)	1710, 1630	1.21 (3H, d, J=7 Hz, C_7-Me), 2.43—4.33 (5H, m, C_7-H, C_8-H, C_9-H, and C_{10}-H), 3.77 (3H, s, NMe), 7.17—7.93 (9H, m, Ar-H)
9	$C_{18}H_{21}NO_3$	72.21 (72.13	7.07 7.23	4.68 4.53)	1730, 1630	*cis*: 1.18 (3H, s, C_8-Me), 1.22 (3H, d, J=7 Hz, C_7-Me), 1.80—2.36 (2H, m, C_9-H), 2.48—3.12 2H, m, C_{10}-H), 3.42 (1H, q, J=7 Hz, C_7-H), 3.52 (3H, s, OMe), 3.68 (3H, s, NMe), 7.12—7.84 (4H, m, Ar-H) *trans*: 1.16 (3H, d, J=7 Hz, C_7-Me), 1.18 (3H, s, C_8-Me), 1.80—2.36 (2H, m, C_9-H), 2.48—3.12 (2H, m, C_{10}-H), 3.42 (1H, q, J=7 Hz, C_7-H), 3.72 (3H, s, NMe), 3.76 (3H, s, OMe), 7.12—7.84 (4H, m, Ar-H)

CH_3), 3.74 (3H, s, NCH_3), 3.97 (3H, s, OCH_3), 7.10—7.50 (3H, m, C_2-H, C_3-H, and C_4-H), 7.08 (1H, d, $J=8$ Hz, C_9-H), 8.17—8.30 (1H, m, C_1-H), 8.43 (1H, d, $J=8$ Hz, C_{10}-H).

π-Allyl Palladium Complex 11——A suspension of sodium acetate (3.6 g, 44 mmol) and palladium sodium chloride (1 g, 3.4 mmol) in a mixture of glacial acetic acid (40 ml) and acetic anhydride (5 ml) was stirred for 2 h at 95 °C. The mixture was cooled to 60 °C, then a solution of **2** (1.6 g, 7.8 mmol) in acetic acid (5 ml) was added in one portion. The reaction mixture was kept at 60 °C for 24 h, and cooled to room temperature. The insoluble material was filtered off. After aqueous work-up and extraction with chloroform, the chloroform layer was dried over sodium sulfate. The solvent was removed and the resulting residue was subjected to silica gel column chromatography using chloroform as an eluent. The chloroform eluate gave a yellow crystalline product, which was recrystallized from a mixture of hexane and benzene to give the product **11** as prisms (635 mg, 55%), mp 190 °C (dec.). *Anal.* Calcd for $C_{26}H_{24}Cl_2N_2O_2Pd_2$: C, 46.14; H, 3.58; N, 4.14. Found: C, 46.30; H, 3.82; N, 4.27. IR ($CHCl_3$): 1645 cm^{-1}. ^1H-NMR ($CDCl_3+CF_3CO_2H$) δ: 3.20 (1H, d, $J=3$ Hz, C_2-methylene proton), 3.36 (3H, s, NCH_3), 3.79 (1H, dd, $J=6$ Hz, $J=3$ Hz, C_{2a}-H), 3.85 (1H, d, $J=3$ Hz, C_2-methylene proton), 4.43 (1H, dd, $J=6$ Hz, $J=3$ Hz, C_{8b}-H), 5.18 (1H, dd, $J=3$ Hz, $J=3$ Hz, C_1-H), 6.87—7.60 (4H, m, aromatic protons).

2-(2,2-Bis(ethoxycarbonyl)ethyl)-4-methyl-3-oxo-2a,3,4,8b-tetrahydrocyclobuta[*c*]quinoline (12)——A solution of **11** (285 mg, 0.42 mmol) and triphenyl phosphite (520 mg, 1.67 mmol) in tetrahydrofuran (THF) (5 ml) was stirred at room temperature for 15 min. In a separate flask, sodium hydride (80.5 mg, 3.35 mmol) was suspended in THF (5 ml), and diethyl malonate (536 mg, 3.35 mmol) was added in one portion. After being stirred for 10 min, the mixture was added under a stream of nitrogen to the solution of the palladium-phosphite complex. The resulting mixture was stirred at room temperature for 2 h. The filtrate of the reaction mixture through Celite was poured into water (100 ml) and the oily layer that separated was extracted with ether. The ether layer was dried over magnesium sulfate. After removal of the solvent *in vacuo*, the oily residue was chromatographed over silica gel. Elution with benzene–ethyl acetate (10 : 1) gave a crystalline product, which was recrystallized from petroleum ether to give the product **12** as prisms (164 mg, 55%), mp 64—65 °C. *Anal.* Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92. Found: C, 67.12; H, 6.63; N, 3.96. IR ($CHCl_3$): 1745, 1725, 1640 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.20 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.26 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 2.59 (2H, d, $J=8$ Hz, $C\underline{H}_2CH$), 3.36 (3H, s, NCH_3), 3.51 (1H, t, $J=8$ Hz, $CH_2C\underline{H}$), 3.66—4.10 (2H, m, C_{2a}-H and C_{8b}-H), 4.16 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 4.22 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 5.80—5.90 (1H, br s, C_1-H), 6.87—7.50 (4H, m, aromatic protons).

(*E*)-2-(Ethoxycarbonylmethylene)-4-methyl-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline ((*E*)-13) and Its Isomer (*Z*)-13——a) A solution of *cis*-**4** (289 mg, 1 mmol) in thionyl chloride (1.5 ml)–dry pyridine (6 ml) was stirred with ice-cooling for 20 h. The reaction mixture was poured into water (30 ml) and the organic layer was extracted with ether. The ether layer was dried over sodium sulfate and concentrated. The oily residue was subjected to silica gel column chromatography using a mixture of hexane–ethyl acetate as an eluent. The hexane–ethyl acetate (8 : 1) eluate gave a crystalline product, which was recrystallized from hexane to give the product (*Z*)-**13** as needles (12 mg, 4%), mp 122.5—123.5 °C. *Anal.* Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.75; H, 6.33; N, 5.19. IR ($CHCl_3$): 1710, 1650 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.33 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 2.93—3.74 (3H, m, C_1-H and C_{8b}-H), 3.37 (3H, s, NCH_3), 4.26 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 4.84—5.13 (1H, m, C_{2a}-H), 5.64—5.77 (1H, m, $C=CHCO$), 6.84—7.43 (3H, m, aromatic protons), 7.67—7.87 (1H, m, aromatic proton). Elution was continued with the same solvent to give (*E*)-**13** as needles (from hexane) (180 mg, 66%), mp 115—116 °C. *Anal.* Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.80; H, 6.26; N, 5.01. IR ($CHCl_3$): 1710, 1650 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.23 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 3.17—4.36 (4H, m, C_1-H, C_{2a}-H, and C_{8b}-H), 3.36 (3H, s, NCH_3), 4.10 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 5.56—5.74 (1H, m, $C=CHCO$), 6.84—7.46 (4H, m, aromatic protons).

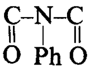
b) Following a procedure similar to that given for *cis*-**4**, *trans*-**4** (289 mg, 1 mmol) was treated with thionyl chloride (1.5 ml)–dry pyridine (6 ml) to give the products (*E*)-**13** (136 mg, 50%) and (*Z*)-**13** (25 mg, 9%).

2-(Ethoxycarbonylmethyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclobuta[*c*]quinoline (14)——A mixture of compounds (*E*)-**13** and (*Z*)-**13** (2.71 g, 0.01 mol) (prepared from *cis*- (or *trans*-) **4**) in sodium ethoxide (0.68 g, 0.01 mol)–dry benzene (10 ml) was stirred at room temperature for 45 min. Water was added to the reaction mixture, and the benzene layer that separated was dried over sodium sulfate. After removal of the solvent under reduced pressure, the resulting residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (4 : 1) gave a crystalline product, which was recrystallized from hexane to give the product **14** as needles (1.1 g, 40%), mp 100—102 °C. *Anal.* Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.77; H, 6.35; N, 5.02. IR ($CHCl_3$): 1725, 1660, 1625 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.26 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 2.70—2.97 (2H, m, CH_2CO), 2.85 (1H, dd, $J=14$ Hz, $J=1$ Hz, C_1-Ha), 3.45 (1H, dd, $J=14$ Hz, $J=4$ Hz, C_1-Hb), 3.57—4.00 (1H, m, C_2-H), 3.70 (3H, s, NCH_3), 4.20 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.07—7.67 (4H, m, aromatic protons).

Reaction of Compound 14 with Olefins: General Procedure——A solution of **14** (100 mg, 0.37 mmol) and olefin (11.1 mmol) in xylene (20 ml) was refluxed. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography to give 7-(ethoxycarbonylmethyl)-5,6,7,8,9,10-hexahydrophenanthridine derivatives **15**—**18**. The results are summarized in Tables III and IV.

7-(Ethoxycarbonylmethyl)-8-methoxycarbonyl-5-methyl-6-oxo-5,6-dihydrophenanthridine (19)——A solution of **15** (179 mg, 0.5 mmol) and DDQ (227 mg, 1 mmol) in dry benzene (5 ml) was refluexed for 45 h. The precipitates were

TABLE III

Product No.	R	R′	R″	Reaction time (h)	Eluent in silica gel column chromatography	Solvent for recrystallization	mp (°C)	Yield (%)
15	H	H	CO_2Me	15	Hexane–ethyl acetate (6:1)	Hexane	148—150	91
16	H	H	CN	15	Hexane–ethyl acetate (4:1)	Hexane–ether	144—145	70
17	 $C(=O)-N(Ph)-C(=O)$		H	11	—	Benzene	228—230 (dec.)	90
18	H	Me	CO_2Me	17	Hexane–ethyl acetate (4:1)	Petroleum ether	101—104	87[a]

a) Mixture of *cis* and *trans*.

TABLE IV

Product No.	Formula	Analysis (%) Calcd (Found) C	H	N	IR ($CHCl_3$) cm^{-1}	NMR ($CDCl_3$) δ
15	$C_{20}H_{23}NO_5$	67.21 (67.27	6.49 6.45	3.92 3.94)	1720, 1630	1.21 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.87—2.36 (3H, m, C_8-H and C_9-H), 2.46—3.07 (4H, m, CH_2CO and C_{10}-H), 3.70 (6H, s, OMe and NMe), 4.10—4.36 (1H, m, C_7-H), 4.13 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.10—7.56 (3H, m, Ar-H), 7.77—8.03 (1H, m, Ar-H)
16	$C_{19}H_{20}N_2O_3$	70.35 (70.45	6.22 6.19	8.64 8.61)	2250, 1725 1640	1.30 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.93—3.37 (7H, m, CH_2CO, C_8-H, C_9-H, and C_{10}-H), 3.74 (3H, s, NMe), 4.03—4.40 (1H, m, C_7-H), 4.28 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.13—7.60 (3H, m, Ar-H), 7.74—7.97 (1H, m, Ar-H)
17	$C_{26}H_{24}N_2O_5$	70.25 (70.16	5.44 5.34	6.30 6.16)	1715, 1625	1.00 (3H, t, $J=7$ Hz, $C\underline{H}_2CH_3$), 2.17—3.57 (6H, m, CH_2CO, C_8-H, C_9-H, and C_{10}-H), 3.77 (3H, s, NMe), 3.87 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 4.46—4.87 (1H, m, C_7-H), 7.20—7.64 (8H, m, Ar-H), 7.93—8.20 (1H, m, Ar-H)
18	$C_{21}H_{25}NO_5$	67.90 (67.69	6.78 6.79	3.77 3.70)	1730, 1630	*cis*: 1.24 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.30 (3H, s, C_8-Me), 1.92—2.20 (2H, m, C_9-H), 2.24—3.08 (4H, m, CH_2CO and C_{10}-H), 3.54 (3H, s, OMe), 3.68 (3H, s, NMe), 3.88—4.08 (1H, m, C_7-H), 4.12 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.16—7.64 (3H, m, Ar-H), 7.96—8.12 (1H, m, Ar-H) *trans*: 1.22 (3H, s, C_8-Me), 1.24 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.92—2.20 (2H, m, C_9-H), 2.24—3.08 (4H, m, CH_2CO and C_{10}-H), 3.68 (3H, s, NMe), 3.72 (3H, s, OMe), 3.88—4.08 (1H, m, C_7-H), 4.12 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.16—7.64 (3H, m, Ar-H), 7.96—8.12 (1H, m, Ar-H)

filtered off and the filtrate was concentrated *in vacuo*. The resulting residue was chromatographed over silica gel. Elution with hexane–ethyl acetate (5 : 1) gave a crystalline product, which was recrystallized from a mixture of hexane and ether to give the product **19** as leaves (33 mg, 19%), mp 91—93 °C. *Anal.* Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.72; H, 5.43; N, 3.88. IR ($CHCl_3$): 1730, 1645 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.31 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 3.74 (3H, s, NCH_3), 3.93 (3H, s, OCH_3), 4.28 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 4.50 (2H, s, CH_2CO), 7.13—7.60 (3H, m, C_2-H, C_3-H, and C_4-H), 7.90—8.10 (1H, m, C_1-H), 8.10 (1H, d, $J=8$ Hz, C_9-H), 8.56 (1H, d, $J=8$ Hz, C_{10}-H).

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References and Notes

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7) By means of a procedure similar to that given for compound **3**,[2] *cis*- and *trans*-**4** were obtained by treatment of **2** with absolute ethanol saturated with dry hydrogen chloride. *cis*-**4**; mp 107—108 °C. IR ($CHCl_3$) of $C_{16}H_{19}NO_4$: 3475, 1710, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.07 (3H, t, $J=7$ Hz, $CH_2\,C\underline{H}_3$), 2.36 (2H, s, CH_2CO), 2.53—3.53 (3H, m, C_1-H and C_{2a}-H), 3.40 (3H, s, NCH_3), 3.63—4.13 (1H, m, C_{8b}-H), 3.83 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 4.60—5.07 (1H, br, OH), 6.77—7.43 (4H, m, aromatic protons). *trans*-**4**; mp 142—143 °C. IR ($CHCl_3$) of $C_{16}H_{19}NO_4$: 3500, 1715, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 2.33 (1H dd, $J=12$ Hz, $J=8$ Hz, C_1-H_a), 2.64—3.36 (2H, m, C_{2a}-H and OH), 2.75 (2H, s, CH_2CO), 2.84 (1H, dd, $J=12$ Hz, $J=1$ Hz, C_1-H_b), 3.36 (3H, s, NCH_3), 3.60—3.87 (1H, m, C_{8b}-H), 4.20 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 6.87—7.46 (4H, m, aromatic protons).