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Photoinduced Molecular Transformations. Part 159.¹ Formation of Some Furonaphthyridinones by Selective β -Scission of Cyclobutanoxyl Radicals Generated From [2+2] Photoadducts of 4-Hydroxy-1-phenyl [1,8] naphthyridin-2(1*H*)-one with Alkenes

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Abstracts: The [2+2] photoaddition of 4-hydroxy-1-phenyl[1,8]naphthyridin-2(1*H*)-one **7** with various alkenes in methanol gave regioselectively the corresponding *head-to-tail* adducts (**8**, **9**, and **11**). The photolysis of the hypiodites generated by the *in situ* reaction of the cyclobutanol adducts **8**, **9**, and **11** with excess mercury(II) oxide-iodine reagent in benzene induced a regioselective scission of their non-ring junction bond of the corresponding alkoxy radicals to give substituted 3,9-dihydro-9-phenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one (**12** and **15**) and/or substituted 3,5-dihydro-5-phenylfuro[3,2-*c*][1,8]naphthyridin-4-(2*H*)-one (**13**, **14**, and **16**). An unusual byproduct **12a** was formed in the photolysis of the hypiodite of the [2+2] photoadduct **8a** of 4-hydroxy-1-phenyl [1,8]naphthyridin-2-(1*H*)-one with isobutene. Copyright © 1996 Elsevier Science Ltd

We have shown that a variety of molecules, including natural products, can be synthesized using the β -scission of alkoxy radicals, generated by the photolysis of hypiodites of appropriate alcohols or lactols, as the key step.² As part of the investigations we have reported on a new radical process by which a hydroxyl oxygen of a fused cyclobutanol is incorporated into the cyclobutane to give a fused furan.³ The reaction was found to be useful for attaching a furan ring to some heteroaromatics, such as coumarin and 2-quinolinone, by combining the process with a [2+2] photoaddition with alkenes.³ Thus, several furoheteroaromatics have been prepared *via* the following two principal processes: (i) the [2+2] photoaddition of heteroaromatics, such as 3- or 4-hydroxycoumarin **1** ($Z=O$),^{3a,c} 4-hydroxyquinolin-2(1*H*)-one **1** ($Z=NMe$),^{3b} and 4-hydroxyisoquinolin-1-(2*H*)-one,^{3d} with alkenes **2** to give the cyclobutanols **3**; (ii) a regioselective β -scission of the alkoxy radicals **A** generated from the cyclobutanols by the photolysis of the corresponding hypiodites **4** (prepared by an *in situ* reaction of the cyclobutanols **3** with mercury(II) oxide-iodine reagent) and a spontaneous recyclization of the resulting carbon-centred radical **B** to give furanoheterocycles (**5** and/or **6**), as outlined in Scheme 1.³

In order to further examine the substrate-product relationship of this new reaction and to develop the synthetic potential of this transformation we have extended the annulation to [1,8]naphthyridin-2(1*H*)-one, and we report here the results in full.

A number of derivatives of the furonaphthyridines have been prepared from the viewpoint of their pharmacological activity.⁴

RESULTS

*Preparations of Cyclobutanols 8a-c, 9b, c and 11 by the [2+2] Photoaddition of 4-Hydroxyphenyl [1,8]naphthyridin-2(1*H*)-one 7 with Isobutene 2a, Ethyl Vinyl Ether 2b, Isopropenyl Acetate 2c, and 1-Methoxy-1-cyclohexene 10 (Schemes 2 and 3).* — The irradiation of 4-hydroxy-1-phenyl [1,8]naphthyridin-2(1*H*)-one **7**⁵ with an excess amount of isobutene **2a** in methanol for 15h with Pyrex-filtered light gave an exclusive photoadduct **8a** in 95% yield (Scheme 2). The structure was established to be (2 α ,8 $\beta\alpha$)-(±)-2,2a,4,8b-tetrahydro-8b-hydroxy-1,1-dimethyl-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one **8a** on the basis of an analysis of the ¹H NMR spectrum. The presence of a signal at δ 3.58 (dd) assignable to C(2a)-H indicated that the *gem*-dimethyl groups are attached to C(1), and that product **8a** is a head-to-tail adduct. The cyclobutane and 6-membered ring should be more stable *cis*-fused on steric grounds, since the cycloadduct was stable for a base.

The photoaddition of naphthyridinone **7** with vinyl ether **2b** under similar conditions gave a pair of head-to-tail cycloadducts, **8b** and **9b**, in 37 and 43% yields (Scheme 2). The ¹H NMR spectra indicated that they are stereoisomers with respect to the C(1) substituents; their 2a-H appeared as a multiplet at δ 3.58 and a doublet of a doublet at δ 3.03, respectively. The 4/6 rings of cycloadducts **8b** and **9b** should also be *cis*-fused, since they were stable for a base. The NOE measurements indicated that the 2a-H and ethoxyl group attached to C(1) of product **9b** are *cis* oriented; the irradiation of a signal at δ 3.03 resulted in an enhancement of the signal areas at δ 4.14 (dd) and δ 2.52 (ddd) assignable to 1a-H and 2a-H, while irradiation of the signal at δ 4.14 caused an enhancement of the signal areas at δ 3.03 and 2.52.

In contrast, the photoaddition of naphthyridinone **7** with isopropenyl acetate **2c** under conditions similar to the above gave a single head-to-tail photoadduct in 76.6% yield (Scheme 2). The ¹H NMR spectrum indicated that the OAc and Me substituents were attached to C(1), since a signal at δ 3.25 attributable to C(2a)-H appeared as a doublet of a doublet. However, whether the structure was **8c** or **9c** remained undefined.

Finally, the photoaddition of naphthyridinone **7** with 1-methoxy-1-cyclohexene **10**⁶ gave a cyclobutanol **11** as the major photoadduct, (as outlined in Scheme 3). The ¹H NMR spectrum exhibited a doublet at δ 3.03 (*J* 10.56) attributable to 6a-H. These NMR spectral data indicated that the cyclobutanol **11** was *cis-transoid-cis* isomer by comparing it with those of 6a-H of (6 α ,6 $\beta\beta$,10 $\alpha\beta$,10 $\beta\alpha$)-(±)-6a,6 β ,7,8,9,10,10a,10b-octahydro-10b-acetoxy-5-methylbenzo[3,4]cyclobuta[1,2-*c*]quinolin-6(5*H*)-one, [obtained by the cycloaddition of 4-acetoxyquinolin-2(1*H*)-one with cyclohexene], the structure of which was determined by an x-ray crystallographic analysis^{3b}, and its *cis-cisoid-cis* isomer.^{3b}

*Formation of Furo [2,3-*b*] and [3,2-*c*][1,8]naphthyridin-4-(2*H*)-ones via β -Scission of Cyclobutanoxyl Radicals Generated from the Photoadducts (Schemes 4-7)*—The irradiation of cyclobutanol **8a** in benzene

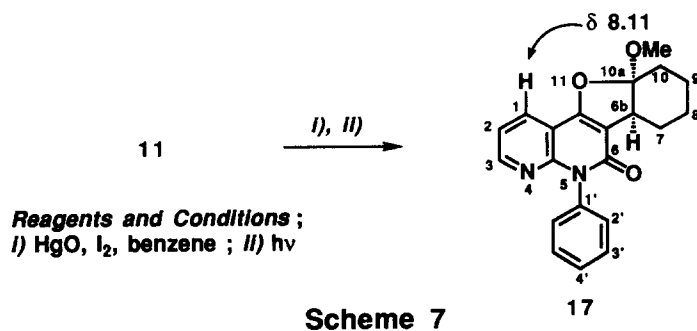
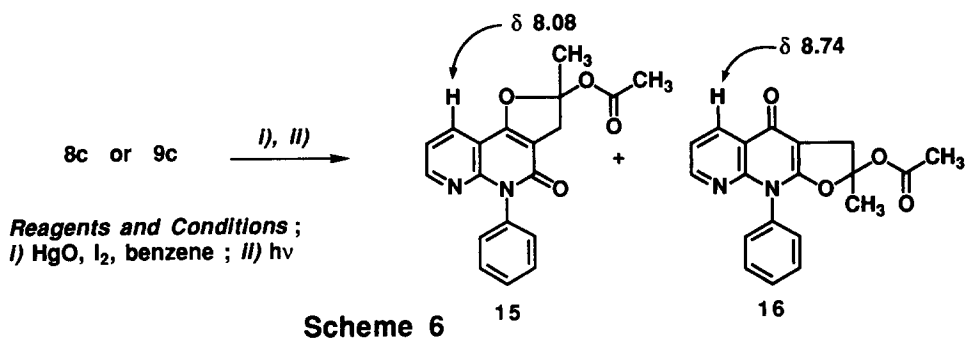
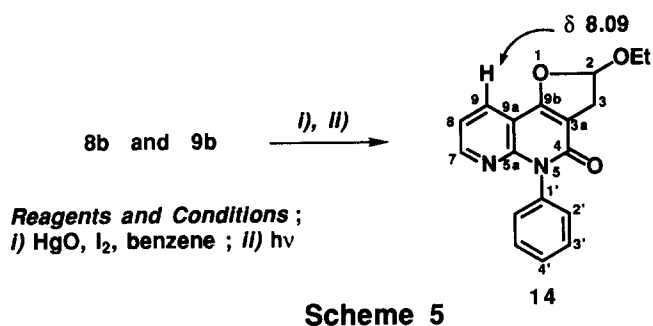
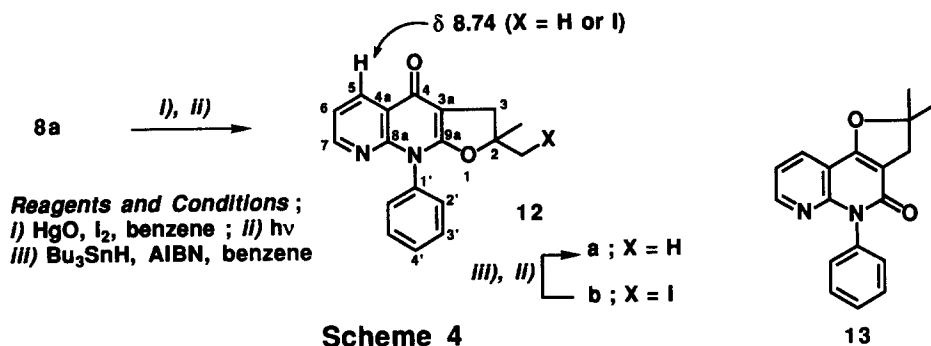


Table 1 ^{13}C and 2-D NMR data for product 12a

Carbon atom ^a	δ_{C} / ppm ^b	DEPT	^1H - ^{13}C COSY Correlation (δ_{H}) ^b
C-2	92.5	C	3.13
C-3	39.2	CH ₂	
C-3a	99.7	C	
C-4	173.7	C	
C-4a	135.1	C	8.74
C-5	135.2	CH	
C-6	119.5	CH	
C-7	150.6	CH	
C-8a	161.2	C	7.26-7.36
C-9a	120.7	C	
C-2-CH ₃	28.1	CH ₃	
C-1'	149.9	C	
C-2' }	{ 129.2	CH	7.26-7.36
C-3' }	{ 129.0		
C-4' }	{ 128.8		

a ; The numbering used here is as shown in the structure in Scheme 4.

b ; δ_{C} and δ_{H} values in CDCl_3 .

Table 2 ^{13}C and 2-D NMR data for product 15

Carbon atom ^a	δ_{C} / ppm ^b	DEPT	^1H - ^{13}C COSY Correlation (δ_{H}) ^b
C-2	109.3	C	3.30, 3.43
C-3	40.1	CH ₂	
C-3a	107.4	C	
C-4	160.9	C	
C-5a	159.6	C	8.47
C-7	150.8	CH	
C-8	117.8	CH	
C-9	131.2	CH	
C-9a	114.7	C	7.15
C-9b	151.7	C	
C-1'	137.2	C	
C-2' }	{ 129.4, 129.2	CH ^c	7.24-7.26
C-3' }			
C-4' }			
COCH ₃	168.5, 21.9	C, CH ₃	2.10
CH ₃	26.0	CH ₃	1.99

a ; The numbering used here is as shown in the structure in Scheme 6.

b ; δ_{C} and δ_{H} values in CDCl_3 .

c ; Two of the signals are due to non-equivalent *ortho*-carbons.

containing mercury(II) oxide and iodine (each 3 equiv.) with a 100-W high-pressure Hg arc through a Pyrex-filter for 5h at room temperature gave two products, **12a** and **12b**, in 25.3 and 48.3% yield, as outlined in Scheme 4. A combustion analysis and mass spectrometry of the products indicated that they had the molecular formulae $C_{18}H_{16}N_2O_2$ and $C_{18}H_{15}N_2O_2I$, respectively. The IR spectrum of the product **12a** showed the presence of the enone group of [1,8]naphthyridin-2(1*H*)-one and the absence of a hydroxyl group. The signals due to a proton adjacent to a carbonyl group were lost in the 1H NMR spectrum. These spectral results in conjunction with the formation paths indicated that the structure was either 3,9-dihydro-2,2-dimethyl-9-phenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one **12a** or its angular isomer **13**.

The structure of the product as a linear-type isomer **12a** was established on the basis of IR, 1H NMR, ^{13}C NMR, and 1H - ^{13}C COSY spectral evidence; the IR spectrum exhibited two intense bands at 1623 and 1591 cm^{-1} assignable to the enone group. A comparison of the band positions of the 2,3-furo-4-quinolinones (linear-type) and 3,4-furo-2-quinolinones (angular-type) showed it to be 2,3-furo-4-naphthyridinone **12a**. The linear isomer was also distinguishable from the corresponding angular isomer by the 1H NMR spectra. The aromatic proton (5-H) at the peri-position of the former thus appeared at δ 8.7, while the corresponding proton of the latter appeared at δ 8.1. The ^{13}C NMR spectral data are given in Table 1. The assignments of the signals are based on a distortionless enhancement by a polarization transfer (DEPT) and the 2D homonuclear chemical shift correlation (COSY) spectra. The signals due to the conjugated carbonyl carbon and aromatic C(5) appeared at δ 173.7 and 135.2, 12.3, and 3.6 ppm downfield of the corresponding signals of the angular-type isomer **15** (*vide infra*).

The key features of the IR and 1H NMR spectra of product **12b** were the same as those of product **12a**: the IR spectrum exhibited two intense bands at 1611 and 1592 cm^{-1} . The 1H NMR spectrum exhibited a signal at δ 8.74 assignable to 5-H. These results indicated that the product had a linear-type structure. In addition to these features, the 1H NMR spectrum of product **12b** exhibited a pair of doublet signals at δ 3.42 and 3.48 (J 10.88 Hz) assignable to non-equivalent methylene protons attached to a carbon having an iodine. These spectral results in conjunction with the formation mechanism (*vide infra*) suggested that the structure of product **12b** was 3,9-dihydro-2-iodomethyl-2-methylphenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one. This structure was then confirmed by transforming it into product **12a** by removing the halogen with Bu_3SnH -AIBN.

The photoreactions of either cyclobutanol **8b** or **9b** under conditions similar to those mentioned above gave the same product **14** in the same 38% yield (Scheme 5). The molecular formula of product **14** was determined to be $C_{18}H_{16}N_2O_3$ by combustion analysis and mass spectrometry. The following spectral analysis indicated that the product **14** was 2-ethoxy-3,5-dihydro-5-phenylfuro[3,2-*c*][1,8]naphthyridin-4(2*H*)-one arising from the insertion of a hydroxyl oxygen to the cyclobutane ring; the IR spectrum exhibited intense bands at 1667 and 1589 cm^{-1} assignable to the enone group. The band position was parallel to those of unsaturated lactam groups of 3,4-furo-2-quinolinones (linear-type). In the 1H NMR spectrum, a diagnostic aromatic proton (9-H) at the peri-position on the fused pyridine ring appeared at δ 8.09, *ca.* 0.6 ppm upfield of the signals of the corresponding protons of products, **12a** and **12b**.

While the β -scission of cyclobutanols **8b** and **9b** led to the same single product, the photoreaction of cyclobutanol **8c** or **9c** under the similar conditions gave a pair of products, **15** and **16** in 31 and 21% yield (Scheme 6). A combustion analysis and high-resolution mass spectrometry showed that products **15** and **16** were isomers having the molecular formula $C_{19}H_{16}N_2O_4$. The structures of these products, **15** and **16**, were

confirmed to be 2-acetoxy-3,5-dihydro-2-methyl-5-phenylfuro[3,2-*c*][1,8]naphthyridin-4(2*H*)-one and its linear fused isomer on the basis of their IR, ^1H NMR, ^{13}C NMR, and ^1H - ^{13}C COSY spectra and the formation mechanism. The IR spectrum of **15** exhibited an intense band at 1675 and 1590 cm^{-1} assignable to the α,β -unsaturated lactam carbonyl, while the IR spectrum of **16** showed a band at 1599 and 1588 cm^{-1} assignable to the enamide group (angular-type). Linear and angular-type structures, **15** and **16**, were also clearly discernible by the ^1H and ^{13}C NMR spectra. The aromatic proton at the peri-position of product **15** appeared at δ 8.74, while the corresponding proton of product **16** appeared at δ 8.08, *ca.* 0.6 ppm upfield. The chemical shifts of the peri-protons of these products were parallel to those of the two types of furonaphthyridines, **14**, and **12a** and **12b**, respectively. The ^{13}C NMR Spectral data, which are based on the DEPT and ^1H - ^{13}C COSY spectra, are given in Table 2. The signals due to the lactam carbonyl carbon and aromatic C(9) appeared at δ 161.4 and 131.6, 12.3 ppm and 3.6 ppm upfields of the corresponding signals of the linear-type isomer **12a**.

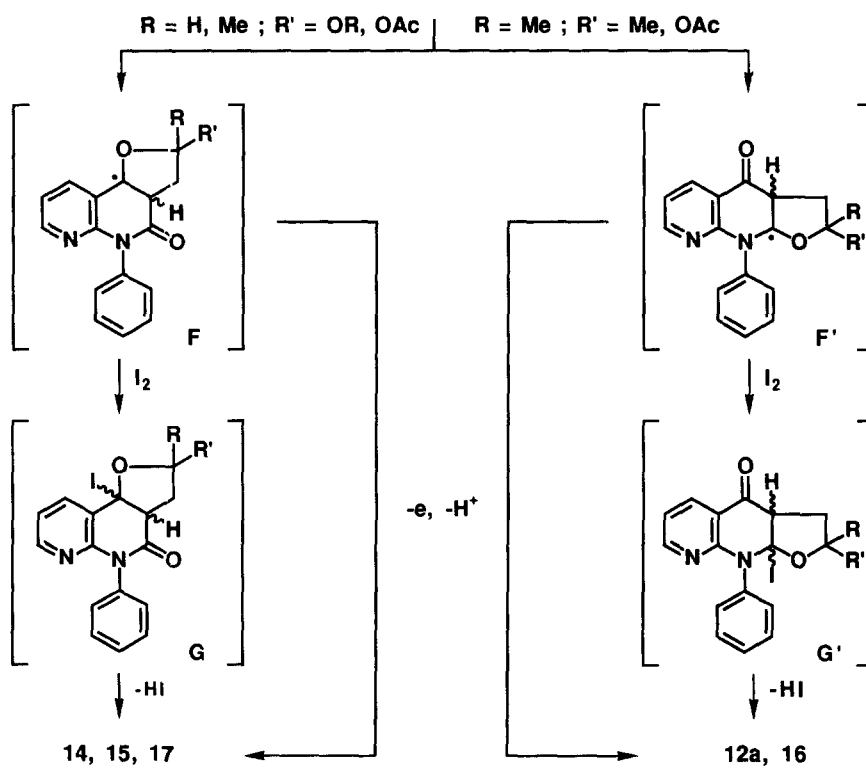
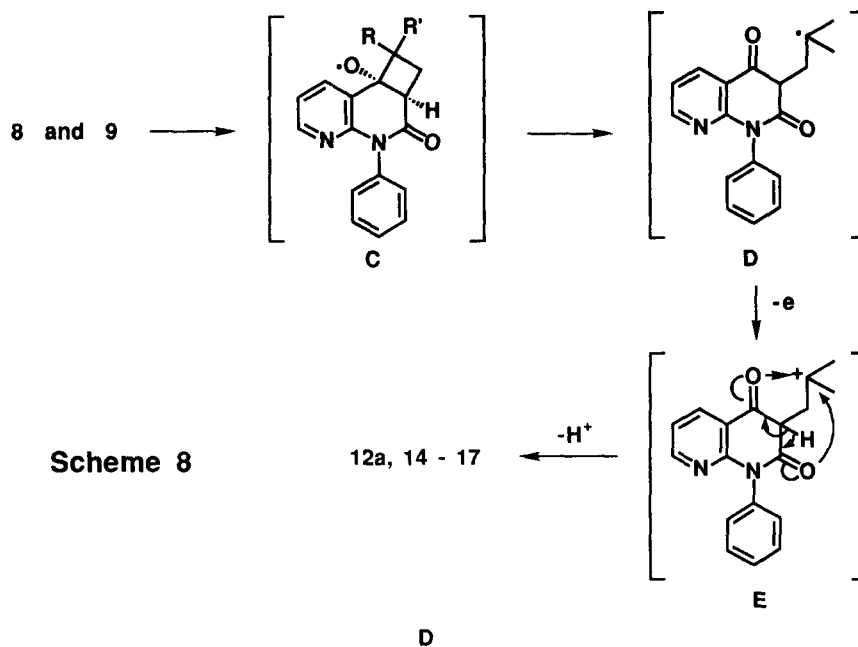
The photolysis of cyclobutanol **11** resulted in the formation of a single product **17** in 61% yield (Scheme 7). The molecular formula of product **17** was established to be $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_3$ by combustion analysis and mass spectrometry. The IR spectrum, which exhibited a band at 1657 and 1587 cm^{-1} assignable to the enone group, and the ^1H NMR spectrum, which exhibited a signal at δ 8.11 assignable to the aromatic proton at the peri-position, indicated that the structure was (6 $\beta\alpha$,10 $\alpha\alpha$)-(\pm)-6 β ,7,8,9,10,10 β -hexahydro-10 α -methoxy-5-phenylbenzofuro[3,2-*c*][1,8]naphthyridin-6(5*H*)-one **17**. A triplet signal at δ 3.43 (*J* 6.94 Hz) in the ^1H NMR spectrum is assignable to the 6 β -H, and the 5/6 ring should be more stable *cis*-fused based on a steric consideration of the formation mechanism.

DISCUSSION

The Photoadditions of 4-Hydroxy-1-phenyl [1,8] naphthyridin-2(1H)-one 7 with Electron-rich Alkenes 2. — The above-mentioned photoadditions of β -hydroxyenone chromophore incorporated in a heterocyclic molecule **7** to unsymmetrical alkenes **2** carrying electron-rich substituents invariably resulted in the formation of head-to-tail adducts, as in the case of the photoaddition of cyclohexenones.^{7,8} The regioselectivity was also parallel to the photoaddition of α - or β -hydroxyenone chromophore incorporated in heterocyclic molecules, such as 3- or 4-hydroxycoumarin^{3a,c} and 4-hydroxyquinolin-2(1*H*)-one.^{3b}

The stereochemical outcome of the photoadditions of enone **7** with electron-rich alkenes was virtually parallel to those of 4-hydroxy-2 quinolone with alkenes previously reported by us;^{3b} the photoaddition of 4-acetoxy-2-quinolone with 1-methoxycycloalkene afforded the *cis-transoid-cis* adduct exclusively, while the photoaddition with cycloalkene afforded *cis-cisoid-cis* adduct exclusively, or a mixture of *cis-cisoid-cis* and *cis-transoid-cis* adducts; the photoaddition of 4-acetoxy-2-quinolone with ethyl vinyl ether in methanol gave two isomeric head-to-tail photoadducts.

It should be noted that in contrast to the [2+2] photoadditions of cyclohexenone with electron-rich alkenes, which produced substantial quantities of 4/6 *trans*-fused photocycloadducts,^{7,8} the [2+2] photoadditions of heteroaromatic enone **7** to alkene **2**,³ including the present examples, invariably resulted in the exclusive formation of the thermodynamically more stable 4/6 *cis*-fused adducts. It is not clear at the present stage whether this difference in stereochemical outcome with the [2+2] photoaddition of cyclohexenones^{7,8} was due to the different mechanisms in the two cases or whether the difference originated

**Scheme 9**

from the greater strains in the twisted relaxed species and the 4/6 *trans*-fused adducts to be derived from the excited aromatic enones in the [2+2] photoadditions.

Paths leading to the Formation of Furonaphthyridinones 12a and 14-17 from the Hypiodites of Cyclobutanols 8, 9, and 11 (Schemes 8 and 9).—The foregoing results showed that cyclobutanols **8**, **9** and **11**, derived from [2+2] photocycloaddition between 4-hydroxy-1-phenyl[1,8]naphthyridin-2(1*H*)-one **7** and various alkenes **2**, gave furo[2,3-*b*][1,8]naphthyridin-4(2*H*)-ones, **12a** and **16** (the linear type), and/or furo[3,2-*c*][1,8]naphthyridin-4(2*H*)-ones, **14**, **15**, and **17** (the angular type), when their benzene solutions containing 3 equiv. each of mercury(II) oxide and iodine were irradiated with Pyrex-filtered light.

The probable paths giving rise to the furonaphthyridinones from the hypiodites of the cyclobutanols **8**, **9**, and **11** are outlined in Schemes 8 and 9. These paths are essentially parallel to those leading to the formation of the furochromones, furocoumarins and furoquinolinones from the cycloadducts of 4-hydroxycoumarin ^{3a} and 4-hydroxy-2-quinolone.^{3b}

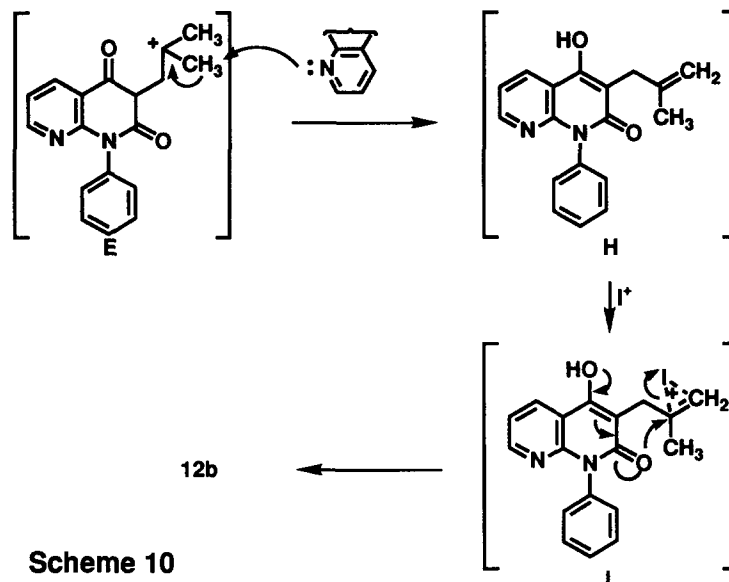
Thus, the alkoxyl radical **C** generated from the cyclobutanol hypiodites gives carbon-centred radical **D**, arising from the selective β-scission of their non-ring junction bond (Scheme 8). There seems to be two probable paths leading to the formation of furonaphthyridinones from the radical **D**. In the first mechanism, furonaphthyridinones **12a**, **14-17** may be formed by the cyclization of an ionic intermediate **E** generated from a one-electron oxidation of the carbon-centred radical **D** (as outlined in Scheme 8).

Alternatively, the furonaphthyridinones can be formed *via* a radical cyclization (as outlined in Scheme 9); an intramolecular combination of carbon-centred radical **D** with either oxygen of the two carbonyls forms cyclic radicals **F** and **F'** from which furonaphthyridinones **12a**, **14-17** are formed through iodides **G** and **G'** or through a one-electron oxidation followed by the loss of a proton, (as outlined in Scheme 9). Of these paths, the formation of an iodide corresponding to the hypothetical intermediates **G** and **G'** has been reported in the photolysis of widdrol hypiodite.⁹

As in the case of the photolysis of the hypiodites of the cyclobutanols derived from the cycloaddition of 4-hydroxycoumarin and 4-hydroxy-2-quinolone, the hypiodites of cyclobutanols **8**, **9** and **11** again resulted in the formation of linear- (**12a**, **12b**, and **16**) and/or angular-type furonaphthyridinones (**14**, **15**, and **17**). The selectivity of the formation of the two types of products including byproduct **12a** was parallel to those in the photolysis of the quinolone series previously reported.^{2b} Thus, the angular-type products were exclusively formed in the photolysis of cyclobutanol adducts carrying an alkoxyl group on the cyclobutane ring, while the linear- type products were exclusive products in the photolysis of cyclobutanol adducts carrying alkyl groups on the cyclobutane ring. The directing effects of the acetoxyl group were again not as powerful as those of the alkoxyl and alkyl groups, and both angular and linear furonaphthyridinones were formed when the cyclobutanol hypiodite carrying the acetoxyl group on the cyclobutane ring was irradiated. Thus, the replacements of C(5) and 4-Me of 4-methylcyclobuta[*c*]quinolin-3(1*H*)-one by a nitrogen and a phenyl group, respectively, did not affect the selectivity for the formation of the two types of furonaphthyridinones.

A Mechanism of The Formation of Byproduct 12b.—A probable mechanism for the formation of a byproduct **12b**, which was not produced in the photolysis of the quinolinone series, is outlined in Scheme 10. It is probably formed through an intermediate alkene **H** produced by removing a proton from the cationic

intermediate **E'** with a base. An intramolecular reaction of an iodonium ion generated from the alkene **H** may give product **12b**. It would be possible that a naphthyridinone, which is more basic than quinolinones, acted as the base.



EXPERIMENTAL

M.p.s were determined with a Yanagimoto micro m.p. apparatus, and are uncorrected. The IR spectra were determined for Nujol mulls with a JASCO IR 810 infrared spectrometer. The ^1H and ^{13}C NMR spectra were determined in CDCl_3 (SiMe_4 as internal reference) with a JEOL JNM-EX 270 spectrometer operating at 270 MHz. High- and low-resolution mass spectra were recorded with a JEOL JMS-DX 303 or a JMS-HX 110. The UV spectrum was recorded with a JASCO Ubest-30 UV/VIS spectrophotometer. PLC was carried out on a Merck Kieselgel 60 PF_{254} . The [2+2] photocycloadditions were carried out with a 500-W High-pressure Hg arc lamp (Eikosha EHB-WI-500). The photolysis of the hypoiodites was carried out with a 100-W high-pressure Hg arc lamp (Eikosha EHB-WU-100).

4-Hydroxy-1-phenyl[1,8]naphthyridin-2(1H)-one 7.—This compound was prepared from 2-chloronicotinic acid according to the procedure of Sherlock *et al.*⁵ 7; λ_{max} (MeOH) / nm : 314 nm (ϵ : 12600) (2.40×10^{-5} mol/l).

[2+2] Photocycloaddition of 4-Hydroxy-1-phenyl[1,8]naphthyridin-2(1H)-one 7.

(i) **With Isobutene 2a.**—A solution of 4-hydroxy-1-phenyl[1,8]naphthyridin-2(1H)-one **7** (150 mg, 0.63 mmol) and isobutene **2a** (1.8 g, 32.1 mmol) in MeOH (71 cm^3) was irradiated through a Pyrex-filter with a 500-W high-pressure Hg arc under nitrogen for 15h at room temperature. Evaporation of the solvent gave a

crude product, which was purified by PLC on silica gel [EtOAc/hexane ; 3/1] to give cyclobutanol **8a**, (2 α , 8 $\beta\alpha$)-(±)-2,2a,4,8b-tetrahydro-8b-hydroxy-1,1-dimethyl-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one **8a** (170 mg, 95 %). m.p. 203-205°C (from EtOAc); (Found: C, 73.45; H, 6.13; N, 9.43. C₁₈H₁₈N₂O₂ requires C, 73.45; H, 6.16; N, 9.52 %); δ_{H} 0.93 (3H, s, Me), 1.41 (3H, s, Me), 1.65 (1H, dd, *J* 9.57 and 11.22, 2-H), 2.24 (1H, dd, *J* 10.22 and 11.22, 2-H), 2.70 (1H, br.s, OH), 3.58 (1H, dd, *J* 9.57 and 10.22, 2a-H), 7.03 (1H, dd, *J* 4.62 and 7.59, 7-H), 7.17 (2H, br.d, *J* 6.93, Ph), 7.38-7.56 (3H, m, Ph), 7.74 (1H, dd, *J* 1.98 and 7.59, 8-H), 8.21 (1H, dd, *J* 1.98 and 4.62, 6-H); $\nu_{\text{max}}/\text{cm}^{-1}$ 3336, 1666; *m/z* (FD) 294 (M⁺, 29), 238 [(M-C₄H₈)⁺, 100].

(ii) *With Ethyl Vinyl Ether 2b*. —A solution of naphthyridinone **7** (50 mg, 0.21 mmol) and ethyl vinyl ether **2b** (1.0 cm³, 10.5 mmol) in MeOH (23.6 cm³) was irradiated for 3h as described above. Evaporation of the solvent gave a mixture of products which was separated by PLC on silica gel [EtOAc/hexane ; 3/1] to give a more mobile fraction, (1 α , 2 $\alpha\alpha$, 8 $\beta\alpha$)-(±)-1-ethoxy-2,2a,4,8b-tetrahydro-8b-hydroxy-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one **8b** (24 mg, 37 %) and a less mobile fraction, (1 α , 2 $\alpha\beta$, 8 $\beta\beta$)-isomer **9b** (28 mg, 43 %).

8b; m.p. 166-168°C (from EtOAc); (Found: C, 69.48; H, 5.87; N, 8.96. C₁₈H₁₈N₂O₃ requires C, 69.66; H, 5.85; N, 9.03 %); δ_{H} 1.30 (3H, t, *J* 6.93, Me), 2.27 (1H, ddd, *J* 5.94, 7.92 and 12.86, 2-H), 2.52 (1H, ddd, *J* 2.97, 10.89 and 12.86 Hz, 2-H), 3.58 (3H, m, OCH₂ and 2a-H), 4.07 (1H, ddd, *J* 0.99, 2.97 and 5.94, 1-H), 4.18 (1H, br.s, OH), 7.04 (1H, dd, *J* 4.62 and 7.58, 7-H), 7.19 (2H, br.d, *J* 7.43, Ph), 7.38-7.54 (3H, m, Ph), 7.84 (1H, dd, *J* 1.98 and 7.58, 8-H), 8.20 (1H, dd, *J* 1.98 and 4.62, 6-H); $\nu_{\text{max}}/\text{cm}^{-1}$ 3450 (OH), 1676 (C=O); *m/z* (EI) 310 (M⁺, 1.8), 281 [(M-Et)⁺, 2.2], 264 [(M-EtOH)⁺, 1.3], 251 (0.99), 237 [(M-CH₂CH₂OEt)⁺, 100].

9b; m.p. 189-191°C (from AcOEt); (Found: C, 69.58; H, 5.93; N, 9.13. C₁₈H₁₈N₂O₃ requires C, 69.66; H, 5.85; N, 9.03 %); δ_{H} 1.18 (3H, t, *J* 6.93, Me), 1.57 (1H, dt, *J* 9.24 and 10.55, 2-H), 2.52 (1H, ddd, *J* 7.92, 9.24 and 10.55, 2-H), 3.03 (1H, dd, *J* 9.24 and 10.55, 2a-H), 3.51 (1H, br.s, OH), 3.53-3.72 (2H, m, OCH₂), 4.14 (1H, dd, *J* 7.92 and 10.55, 1-H), 7.04 (1H, dd, *J* 4.95 and 7.59, 7-H), 7.12 (2H, br.d, *J* 7.26, Ph), 7.35-7.55 (3H, m, Ph), 7.85 (1H, dd, *J* 1.98 and 7.59, 8-H), 8.21 (1H, dd, *J* 1.98 and 4.95, 6-H); $\nu_{\text{max}}/\text{cm}^{-1}$ 3406 (OH), 1672 (C=O); *m/z* (EI) 310 (M⁺, 0.83), 281 [(M-Et)⁺, 2.2], 264 [(M-EtOH)⁺, 1.1], 251 (0.9), 237 [(M-CH₂CH₂OEt)⁺, 100].

(iii) *With Isopropenyl Acetate 2c*. —A solution of naphthyridine **7** (100 mg, 0.42 mmol) and isopropenyl acetate **2c** (2.3 cm³, 20.99 mmol) in MeOH (47.2 cm³) was irradiated for 6h in a similar manner as mentioned above. After evaporation of the solvent, the crude product was purified by PLC on silica gel [hexane/EtOAc ; 1/3] to give a product **8c** or **9c** (108.8 mg, 76.6 %), (2 $\alpha\alpha$, 8 $\beta\alpha$)-(±)-1-acetoxy-2,2a,4,8b-tetrahydro-8b-hydroxy-1-methyl-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one. m.p. 263-264°C (from MeOH); (Found: C, 67.43; H, 5.35; N, 8.32. C₁₉H₁₈N₂O₄ requires C, 67.44; H, 5.37; N, 8.32 %); δ_{H} 1.75 (s, 3H, Me), 1.85 (3H, s, MeCOO-), 2.06 (1H, t, *J* 11.22, 2-H), 2.78 (1H, dd, *J* 9.57 and 11.22, 2-H), 3.07 (1H, s, OH), 3.25 (1H, dd, *J* 9.57 and 11.22, 2a-H), 7.05 (1H, dd, *J* 4.62 and 7.76, 7-H), 7.15 (2H, br.d, *J* 6.93, Ph), 7.25-7.53 (3H, m, Ph), 7.92 (1H, dd, *J* 1.98 and 7.76, 8-H), 8.24 (1H, dd, *J* 1.98 and 4.62, 6-H); $\nu_{\text{max}}/\text{cm}^{-1}$ 3434 (OH), 1732 (OC=O), 1673 (C=O); *m/z* (EI) 338 (M⁺, 0.57), 277 (51.3), 237 [(M-C₂H₃CH₃OAc)⁺, 100].

(iv) **With 1-Methoxy-1-cyclohexene 10.**⁶—Irradiation of a solution of naphthyridine **7** (100 mg, 0.42 mmol) and 1-methoxy-1-cyclohexene **10** (2.6 cm³) in MeOH (47.2 cm³) was carried out in a similar manner as above for 3h. After evaporation of the solvent, a residue was separated by PLC on silica gel [CH₂Cl₂/MeOH ; 80/1, 50/1 × 2] to give (6aα,6bβ,10aβ,10bα)-(±)-6a,6b,7,8,9,10,10a,10b-octahydro-10b-hydroxy-10a-methoxy-5-phenylbenzo[3,4]cyclobuta[1,2-*c*][1,8]-naphthyridin-6(5*H*)-one **11** (73.2 mg, 49.8 %) and a mixture (39.1 mg) including (6aα,6bα,10aα,10bα)-isomer (by ¹H NMR).

11; m.p. 236.5-238°C (CHCl₃); (Found. C, 56.28; H, 4.99; N, 6.02; Cl, 22.56. C₂₁H₂₂N₂O₃·CHCl₃ requires C, 56.24; H, 4.94; N, 5.96; Cl, 22.64 %); δ_H (DMSO-*d*₆) 1.23-1.33 (1H, m), 1.51-1.57 (m, 2H), 1.72-1.84 (3H, m), 2.13-2.20 (2H, m), 2.25 (1H, dd, *J* 4.62 and 10.56, 6b-H), 3.03 (1H, d, *J* 10.56, 6a-H), 3.17 (3H, s, OMe), 7.02 (1H, dd, *J* 4.62 and 7.76, 1-H), 7.18 (2H, br.d, *J* 7.26, Ph), 7.37-7.53 (4H, m, Ph and CHCl₃), 7.93 (1H, dd, *J* 1.98 and 7.76, 2-H), 8.16 (1H, dd, *J* 1.98 and 4.62, 3-H); ν_{max}/cm⁻¹ 3364, 1663; *m/z* (FD) 351[(MH)⁺, 100], 238[(M-C₆H₁₀OMe)⁺, 40.9].

General Procedure for the Photolysis of the Hypiodite of Cyclobutanols.—To a solution of a cyclobutanol in benzene (0.02 M), mercury(II) oxide (2 equivalents) and iodine (2 equivalents) were added. The solution was flushed with nitrogen and then irradiated with a 100 W high-pressure Hg arc through a Pyrex-filter at room temperature. The reaction mixture was filtered through Celite and the organic layer was washed successively with 5 % Na₂S₂O₃ solution, water, and saturated brine. After dryness over anhydrous Na₂SO₄ and evaporation of the solvent, the crude product was subjected to PLC to give pure products.

Photolysis of the Hypiodite of Cyclobutanol 8a.—Cyclobutanol **8a** (130 mg, 0.44 mmol) in benzene (22 cm³) containing mercury(II) oxide (287.3 mg, 1.32 mmol) and iodine (336.4 mg, 1.32 mmol) was irradiated for 5h. After usual workup, the crude products were subjected to PLC on silica gel [EtOAc/hexane ; 5/1, 7/1, 10/1 × 2] to give three fractions. The most mobile fraction was a recovered starting cyclobutanol **8a** (16 mg, 12.3 %). The next mobile fraction (41 mg, 22.2 %) was 3,9-dihydro-2-iodomethyl-2-methyl-9-phenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one **12b**. m.p. 168.5-170°C (from acetone); (Found C, 51.88; H, 3.64; N, 6.33; I, 30.12. C₁₈H₁₅N₂O₂I requires C, 51.69; H, 3.62; N, 6.70; I, 30.34 %); δ_H 1.70 (s, 3H, Me), 3.29 (1H, d, *J* 14.52, 3-H), 3.38 (3H, d, *J* 14.52, 3-H), 3.42 (1H, d, *J* 10.88 Hz, CH₂I), 3.48 (1H, d, *J* 10.88, CH₂I), 7.26-7.58 (6H, m, 6H, Ph and 6-H), 8.52 (1H, dd, *J* 1.98 and 4.62, 7-H), 8.74 (1H, dd, *J* 1.98 and 7.91, 5-H); ν_{max}/cm⁻¹ 1623, 1591; *m/z* (FD) 418 (M⁺, 100).

The most polar fraction (54.7 mg, 42.4 %) was 3,9-dihydro-2,2-dimethyl-9-phenylfuro[2,3-*b*][1,8]-naphthyridin-4(2*H*)-one **12a** (54.7 mg, 42.4 %). m.p. 193-195.5°C (from EtOAc); (Found C, 74.10; H, 5.70; N, 9.51. C₁₈H₁₆N₂O₂ requires C, 73.95; H, 5.52; N, 9.58 %); δ_H 1.52 (6H, s, Me × 2), 3.13 (2H, s, 3-H), 7.26-7.36 (3H, m, 6-H and Ph), 7.52-7.61 (3H, m, Ph), 8.50 (1H, dd, *J* 1.98 and 4.62, 7-H), 8.74 (1H, dd, *J* 1.98 and 7.75, 5-H); ν_{max}/cm⁻¹ 1611, 1592; *m/z* (FD) 292 (M⁺, 100), 284 (18.68).

The yields of **12a** and **12b** based on the converted cyclobutanol were 48.3 % and 25.3 %.

Photolysis of the Hypiodite of Cyclobutanol 8b.—Cyclobutanol **8b** (50 mg, 0.16 mmol) in benzene (8.5 cm³) containing mercury(II) oxide (110.5 mg, 0.48 mmol) and iodine (129.4 mg, 0.48 mmol) was irradiated for 5h. After usual workup, the crude products were subjected to PLC on silica gel [acetone/hexane ; 1/1] to give two fractions. The more mobile fraction (15.4 mg, 31 %) was (±)-2-ethoxy-3,5-dihydro-5-

phenylfuro[3,2-*c*][1,8]naphthyridin-4(2*H*)-one **14**. m.p. 159–161°C (from EtOH); (Found C, 68.75; H, 5.49; N, 8.69. $C_{18}H_{16}N_2O_3 \cdot 1/2EtOH$ requires C, 68.86; H, 5.79; N, 8.46 %); δ_H 1.31 (3H, t, *J* 7.26, Me), 3.14 (1H, dd, *J* 2.97 and 17.15, 3-H), 3.41 (1H, dd, *J* 7.26 and 17.15, 3-H), 3.78 (1H, dq, *J* 7.26 and 9.24, OCH_2), 4.06 (dq, *J* 7.26 and 9.24, 1H, OCH_2), 6.08 (dd, *J* 2.97 and 7.26, 1H, 2-H), 7.15 (dd, *J* 4.6 and 7.92, 1H, 8-H), 7.26 (2H, m, Ph), 7.44–7.58 (3H, m, Ph), 8.09 (1H, dd, *J* 1.65 and 7.92, 9-H), 8.47 (1H, dd, *J* 1.65 and 4.62, 7-H); ν_{max}/cm^{-1} 1667 (C=O); *m/z* (EI) 308 (M^+ , 43.8), 263 [(*M*-OEt) $^+$, 100], 251 (64.5).

The less mobile fraction (9.5 mg, 19 %) was recovered starting material. The yields of **14** based on the converted cyclobutanol **8b** was 38 %.

Photolysis of the Hypiodite of Cyclobutanol 9b.—Cyclobutanol **9b** (50 mg, 0.16 mmol) was allowed to react for 2h in the same manner as mentioned above. After the same workup, a residue was subjected to PLC on silica gel [EtOAc/hexane ; 3/1] to give (±)-2-ethoxy-3,5-dihydro-5-phenylfuro [3,2*c*][1,8] naphthyridin - 4(2*H*)-one **14** (12.3 mg, 24.8 %) and recovered starting cyclobutanol **9b** (17.5 mg, 35 %). The yield of product **14** based on the converted cyclobutanol **9b** was 38 %.

Photolysis of the Hypiodite of Cyclobutanol 8c or 9c.—Cyclobutanol **8c** or **9c** (50 mg, 0.14 mmol) in benzene (8.5 cm³) containing mercury(II) oxide (110.5 mg, 0.48 mmol) and iodine (129.4 mg, 0.48 mmol) was irradiated for 2h. After usual workup, the crude products were subjected to PLC on silica gel [EtOAc/hexane 2/1] to give two fractions. The more mobile fraction (25 mg, 31 %) was (±)-2-acetoxy-3,5-dihydro-2-methyl-5-phenylfuro[3,2-*c*][1,8]naphthyridin-4(2*H*)-one **15**. m.p. 183–184°C (from MeOH); (Found C, 67.66; H, 4.88; N, 8.24. $C_{19}H_{16}N_2O_4$ requires C, 67.84; H, 4.80; N, 8.33 %); δ_H 1.99 (s, 3H, Me), 2.10 (3H, s, MeCOO), 3.30 (1H, d, *J* 17.16, 3-H), 3.43 (1H, d, *J* 17.16, 3-H), 7.15 (1H, dd, *J* 4.62 and 7.59, 8-H), 7.24–7.26 (2H, m, Ph), 7.44–7.58 (3H, m, Ph), 8.08 (1H, dd, *J* 1.98 and 7.59, 9-H), 8.47 (1H, dd, *J* 1.98 and 4.62, 7-H); ν_{max}/cm^{-1} 1734 (OAc), 1675 (C=O); *m/z* (EI) 336 (M^+ , 0.12), 294 (5.83), 275 (100), 251 (30.6).

The less mobile fraction (16.4 mg, 21 %) was (±)-2-acetoxy-3,9-dihydro-2-methyl-5-phenylfuro[2,1-*b*][1,8]aphthyridin-4(2*H*)-one **16**. m.p. 96–98°C (from EtOAc-Hexane); (Found: M^+ , 336.1108. $C_{19}H_{16}N_2O_4$ requires *M*, 336.1110); δ_H 1.81 (3H, s, Me), 2.06 (3H, s, MeCOO), 3.34 (1H, d, *J* 15.84, 3-H), 3.48 (1H, d, *J* 15.84, 3-H), 7.32 (1H, dd, *J* 4.62 and 7.92, 6-H), 7.35 (2H, br. d, *J* 1.98, Ph), 7.53–7.59 (3H, m, Ph), 8.53 (1H, dd, *J* 1.98 and 4.62, 7-H), 8.74 (1H, dd, *J* 1.98 and 7.92, 5-H); ν_{max}/cm^{-1} 1720 (OAc), 1687, 1599 (aryl-CO-C=C-); *m/z* (EI) 336 (M^+ , 0.34), 318 (0.19), 294 (2.6), 275 (100).

Photolysis of the Hypiodite of Cyclobutanol 11.—Cyclobutanol **11** (50 mg, 0.14 mmol) in benzene (8.5 cm³) containing mercury(II) oxide (110.5 mg, 0.51 mmol) and iodine (129.4 mg, 0.51 mmol) was irradiated for 2h. After usual workup, the crude products were subjected to PLC on silica gel [EtOAc/hexane 2/1] to give (6*α*,10*α*)-(±)-6*b*,7,8,9,10,10*b*-hexahydro-10*a*-methoxy-5-phenylbenzofuro[3,2-*c*][1,8]-naphthyridin-6(5*H*)-one **17** (30.3 mg, 61 %). m.p. 144–144.5°C (from MeOH); (Found C, 72.23; H, 5.87; N, 8.03. $C_{21}H_{20}N_2O_3$ requires C, 72.39; H, 5.80; N, 8.04 %); δ_H 1.42–1.58 (2H, m, 2H, CH_2), 1.66–1.79 (2H, m, CH_2), 1.92–2.01 (1H, m, CH_2), 2.17–2.31 (2H, m, CH_2), 3.427 (1H, t, *J* 6.94, 6*b*-H), 3.432 (3H, s, OMe), 7.14 (1H, dd, *J* 4.6 and 7.76, 2-H), 7.26 (2H, br. d, *J* 1.65, Ph), 7.28–7.58 (3H, m, Ph), 8.11 (1H, dd, *J* 1.98

and 7.76, 1-H), 8.46 (1H, dd, *J* 1.98 and 4.62, 3-H); $\nu_{\max}/\text{cm}^{-1}$ 1657; m/z (EI) 348 (M^+ , 1.90), 333 [$(\text{M}-\text{Me})^+$, 13.3], 315 (100).

Dehalogenation of Iodide 12b with Bu_3SnH -AIBN.—To a solution of iodide **12b** (60.5 mg, 0.14 mmol) in benzene (7.4 cm^3) was added Bu_3SnH (0.08 cm^3 , 0.28 mmol) and AIBN (11.9 mg, 0.07 mmol). The solution was flushed with nitrogen and then irradiated for 0.5h with a 100 W high-pressure Hg arc through a Pyrex-filter at room temperature. The solvent was then removed by evaporation and to the residue were added diethyl ether (8 cm^3) and KF (17.6 mg, 0.28 mmol). The solution was stirred on overnight and was filtered through Celite. The organic layer was washed with water and then saturated brine. After dryness over anhydrous Na_2SO_4 and evaporation of the solvent, the crude products were subjected to PLC on silica gel [EtOAc/hexane; 10/1 \times 2] to give a dehalogenated product **12a** (27.7 mg, 65.5 %), which was identical with **12a**, obtained in the photolysis of the hypoiodite of cyclobutanol **8a**.

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