Studies on the N-Oxides of π-Deficient N-Heteroaromatics. XXXIV.[1-3]
A Novel Synthesis of Substituted Indoles by Photochemical Ring Contraction of 3,1-Benzoxazepines

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A novel photochemical ring-contraction reaction of 5-unsubstituted 3,1-benzoxazepines and their 5-halogeno or carboxyl derivatives to yield 3-formylindoles in an aprotic solvent is reported. This ring contraction was successfully extended to oxazepines having an alkoxycarbonyl function at the 5-position to give the indoles having this function at the 3-position. Though most of the oxazepines underwent the ring-contraction reaction only on irradiation at 254 nm, 5-carboxy derivatives or their esters afforded the ring-contraction products even at ≥300 nm.

The intermediacy of 3H-indole species in these photochemical ring-contraction reactions was demonstrated by the isolation of methyl 3-acetyl-2-phenyl-3H-indole-3-carboxylate during the photolysis of methyl 4-methyl-2-phenyl-3,1-benzoxazepine-5-carboxylate. It was found that this 3H-indole afforded methyl 6- and 4-acetyl-2-phenyl-indole-3-carboxylates upon further irradiation. The mechanism of this acetyl migration is discussed based on the result of the photochemical acetyl migration of methyl 1-acetyl-2-phenylindole-3-carboxylate.

Keywords——photochemical ring contraction; photochemical rearrangement; photochemical indole synthesis; solvolysis of 3,1-benzoxazepines; photolysis of methyl 1-acetylindole-3-carboxylate; methyl 3-acetyl-3H-indole-3-carboxylate

It is well known that 3,1-benzoxazepine derivatives are formed by irradiation (≥300 nm) of quinoline 1-oxides.[5] While these oxazepines were believed to be stable to further photochemical reactions with a few exceptions,[6] we have now found that irradiation of these oxazepines at 254 nm causes a general ring contraction reaction to give indole derivatives. Thus, 5-unsubstituted 3,1-benzoxazepines, which are stable to ≥300 nm irradiation, afforded 3-formylindoles on irradiation at 254 nm in an appropriate solvent in satisfactory yields. Under the same irradiation condition, 5-chloro-2-cyano-3,1-benzoxazepine afforded not only 2-cyano-3-formylindole but also a series of 2-cyanoindoles chlorinated at various positions in the benzene portion; these were clearly a result of concomitant chlorine migration with the ring contraction. A loss of the 5-substituent in the oxazepine system was also observed in the ring

1) Part XXXIII: C. Kaneko, T. Naito, M. Hashiba, H. Fujii, and M. Somei, *Chem. Pharm. Bull.*, **27**, 1813 (1979).
2) This paper also forms Part X of "Studies on Oxazepine Derivatives." Part IX: C. Kaneko, A. Yamamoto, and M. Hashiba, *Chem. Pharm. Bull.*, **27**, 946 (1979).
3) A part of this work has been published as communications: *a*) C. Kaneko and R. Kitamura, *Heterocycles*, **6**, 111 (1977); *b*) C. Kaneko and R. Kitamura, *ibid.*, **6**, 117 (1977); *c*) R. Kitamura, H. Fujii, K. Hashiba, M. Somei, and C. Kaneko, *Tetrahedron Lett.*, **1977**, 2911.
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5) *a*) C. Kaneko, *Yukigosei Kagaku Kyokaishi* (*J. Syn. Org. Chem. Japan*), **26**, 758 (1968); *b*) M. Ishikawa and C. Kaneko, *Kagaku no Ryoiki*, Suppl. **92**, 149 (1970); *c*) G.G. Spence, E.C. Taylor, and O. Buchardt, *Chem. Rev.*, **70**, 231 (1970); *d*) F. Bellamy and J. Streith, *Heterocycles*, **4**, 1391 (1976).
6) C. Kaneko and S. Yamada, *Chem. Pharm. Bull.*, **14**, 555 (1966); M. Ishikawa, C. Kaneko, and S. Yamada, *Tetrahedron Lett.*, **1968**, 4519.

contraction of oxazepines having a carboxyl function at the 5-position to give 3-formylindoles. It seems noteworthy that this ring contraction reaction proceeded smoothly even on irradiation at ≥ 300 nm.   Similar photo-lability to ≥ 300 nm rays was also observed for 5-methoxy-carbonyl-3,1-benzoxazepines.   Thus, on irradiation at ≥ 300 nm in an aprotic solvent, these oxazepines afforded methyl indole-3-carboxylates in high yields.   The formation of the latter compounds suggested that the ring contraction occurred with concurrent decarbonylation.

The intermediacy of a 3H-indole species, expected to be formed from the oxazepines by a photochemically allowed 1,3-sigmatropic rearrangement (in more general terminology, a $_\pi 2_s +$ $_\sigma 2_s$ pericyclic reaction),[7] was proposed in order to account for the formation of these ring-contraction products and was later demonstrated by successful isolation and characterization of methyl 3-acetyl-2-phenyl-3H-indole-3-carboxylate from the photochemical reaction of methyl 4-methyl-2-phenyl-3,1-benzoxazepine-5-carboxylate.

The Photochemical Ring-contraction Reactions of 5-Unsubstituted 3,1-Benzoxazepines to give 3-Formylindoles

Irradiation of 2-cyano-3,1-benzoxazepine (2a) in acetonitrile gave, after chromatography on silica gel, 3-formyl-2-cyanoindole (3a) in $ca.$ 80% yield as the sole isolable product, this gave the monohydrazone and exhibited characteristic bands due to CN, NH, and CHO groups (2220, 3150, and 1650 cm^{-1}, respectively) in the infrared (IR) spectrum.   The results of elemental analysis and the nuclear magnetic resonance (NMR) spectrum also supported the proposed structure (3a).   In a similar way, two other 3-formylindoles (3b and 3c) were also obtained in satisfactory yields.   The structure of 3c was confirmed by direct comparison with an authentic sample.[8]   As in the case of indole-3-carboxaldehyde, the ultraviolet (UV) maxima of these indoles (3a—c) shift to a longer wavelength region in alkaline solution.[9]   Hence,

	X	Y
1—3		
a	CN	H
b	CN	OCH$_3$
c	C$_6$H$_5$	H
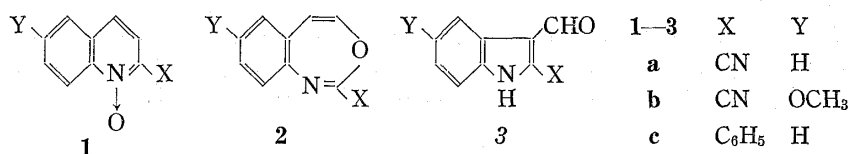
the corresponding quinoline-1-oxides (1a—c) were irradiated in acetonitrile via a Pyrex filter until their disappearance, then the irradiation was continued without the filter until the oxazepines (2a—c) were consumed.   Alternatively, irradiation of the N-oxides without the filter from the beginning afforded 3-formylindoles (3a—c) in $ca.$ 40—70% yields.

Irradiation of 5-Chloro-2-cyano-3,1-benzoxazepine (5) at 254 nm in Acetonitrile

The oxazepine (5), which was obtained in 80% yield by the irradiation of 4-chloro-2-cyanoquinoline 1-oxide[10] (4) at ≥ 300 nm, was irradiated at 254 nm in acetonitrile until its disappearance.   Silica gel chromatography of the products afforded five monochloroindoles (6—10), in addition to 3-formyl-2-cyanoindole (3a).   The least polar product among them was assigned as 3-chloro-2-cyanoindole (6) based on elemental analysis and the UV spectrum, which was quite similar to that of 2-cyanoindole; its NMR spectrum was consistent with the assigned structure (6).   The four other products (7—10) had a common molecular formula of C$_{10}$H$_5$ClN$_2$O and showed UV spectra similar to that of 2-cyano-3-formylindole (3a).   These structures were unequivocally assigned from thier NMR spectra, which easily permitted deduc-

7) R. Hoffmann and R.B. Woodward, $Accounts Chem. Res.$, 1, 17 (1968); R.B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, Inc., New York, N.Y. 1970, p. 169.
8) D.E. Horning and M.J. Muchowski, $Can. J. Chem.$, 48, 1931 (1970).
9) The UV spectra of 3-formylindole and its derivatives (3a—c) in methanol and in alkaline solution were reported in our previous communications.$^{3a)}$
10) This N-oxide was obtained by usual N-oxidation of the corresponding base: C. Kaneko, $Chem. Pharm. Bull.$, 8, 286 (1960).
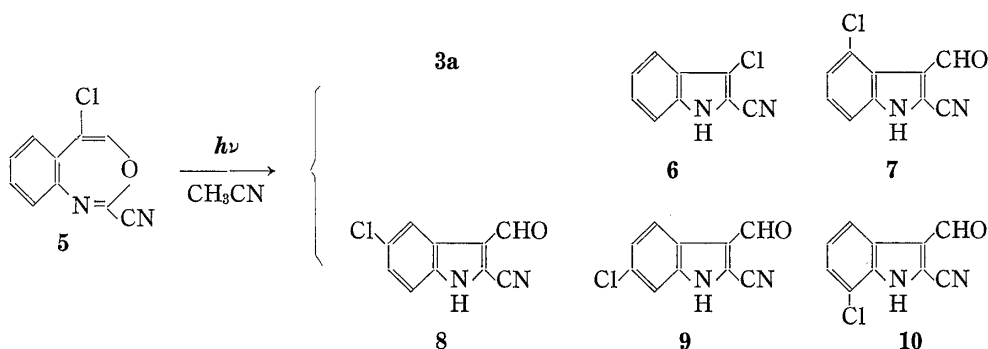
TABLE I. ¹H-NMR Spectra of 2-Cyano-3-formylindole (3a) and Its
Monochlorinated Derivatives (7—10) in DMSO-d_6[a,b]

Comp.	Substituent	H_4	H_5	H_6	H_7	CHO
3a	None	8.19, m	← ——7.3—7.7—— →			10.16, s
7	4-Cl	—	← ——7.4—7.6—— →			10.62, s
8	5-Cl	8.12, d (2.0)	—	7.48, d.d (9.0, 2.0)	7.88, d (9.0)	10.17, s
9	6-Cl	8.20, d (8.5)	7.43, d.d (8.5, 2.0)	—	7.70, d (2.0)	10.19, s
10	7-Cl	8.12, d.d (7.5, 1.0)	7.35, d.d (8.0, 7.5)	7.56, d.d (8.0, 1.0)	—	10.13, s

a) Chemical shifts in δ (in ppm).
b) Coupling constants (in Hz) are shown in parentheses.

tion of the position of the chlorine atom in each product from the couping pattern of the
C_4-proton signal. Table I shows the NMR spectra of **3a** and its chlorinated derivatives
(**7—10**).

Ring Contraction of Quinoline 1-Oxide-4-carboxylic Acids to give 3-Formylindoles

Next, we tried to extend the above ring-contraction reaction to the oxazepine-5-carboxylic
acids. Thus, anticipating the formation of the oxazepines (**12c—e**), a series of quinoline 1-
oxide-4-carboxylic acids (**11c—e**) was irradiated in methanol[11] at ≥300 nm until their disap-
pearance. Quite unexpectedly, 3-formylindoles (**13c, d**) were obtained as the major products,
in addition to 2-quinolone derivatives (**14 and 15**). For example, irradiation of 2-methyl-
quinoline 1-oxide-4-carboxylic acid (**11d**) in methanol resulted in the formation of three major
rearrangement products (**13d, 14d,** and **15d**). The product (**13d**) was confirmed to be 3-formyl-
2-methylindole by mixed melting point determination with an authentic sample.[12] Two
other products (**14d** and **15d**) showed typical carbostyril absorptions in the UV spectra, and
the position of the methyl group in each product was determined from the NMR spectra.
Under the same irradiation conditions, 2-phenylquinoline 1-oxide-4-carboxylic acid (**11c**) also
afforded 3-formyl-2-phenylindole (**13c**) in 59.5% yield, together with 3-phenyl-2-quinolone
4-carboxylic acid[13] (**14c**) as a major by-product.

Based on the results of these photolyses, it seems reasonable to explain the formation
of 3-formylindoles (**13**) in terms of the sequence shown in Chart 1. If this is correct, the
presence of a carboxyl function at the 5-position of the oxazepine system obviously enhances
instability of these oxazepines under irradiation at ≥300 nm. It should also be noted that

11) Since these carboxylic acids (11) are insoluble in ordinary aprotic solvents, we had to use methanol in
    this study.
12) G.F. Smith, *J. Chem. Soc.*, **1954**, 3842.
13) W. Borsche and W. Jacobs, *Chem. Ber.*, **47**, 354 (1914).

Chart 1

11—15	X
c	C_6H_5
d	CH_3
e	H

14   **15**   **16c**
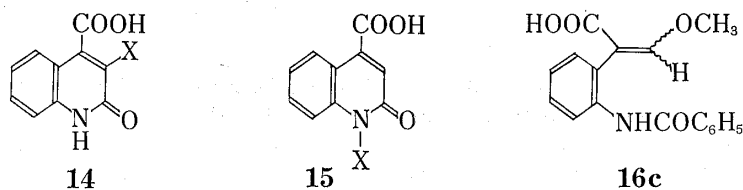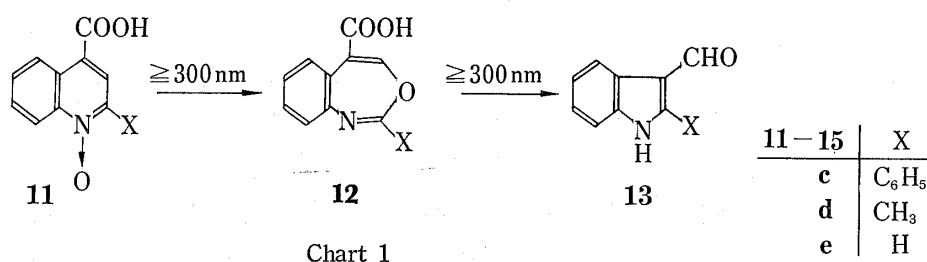
the solvent adduct (**16c**) was obtained from **11c** as a minor by-product.[14] Though we used methanol as the irradiation solvent in these photolyses, the yields of 2-quinolone derivatives were relatively low compared to the photolyses of the N-oxides without a carboxyl function. Thus, while quinoline 1-oxide gave almost exclusively 2-quinolone,[15] 3-formylindole (**13e**) was obtained from **11e** in appreciable yield under these conditions, though the major photoproduct was 2-quinolone-4-carboxylic acid (**14e**).

Ring Contraction of Methyl Quinoline 1-Oxide-4-carboxylates to Methyl Indole-3-carboxylates by Irradiation at ≥300 nm in an Aprotic Solvent

In order to establish the intermediacy of oxazepine species in the photo-ring contraction of the N-oxides (**11**) to 3-formylindoles (**13**) and also to check the stability of the oxazepine system having a carboxyl function to irradiation at ≥300 nm, methyl quinoline 1-oxide-4-carboxylates (**17**) were irradiated at ≥300 nm in an aprotic solvent.[16] When the irradiation

| 17—19	X
f	C_6H_5
g	CH_3

20
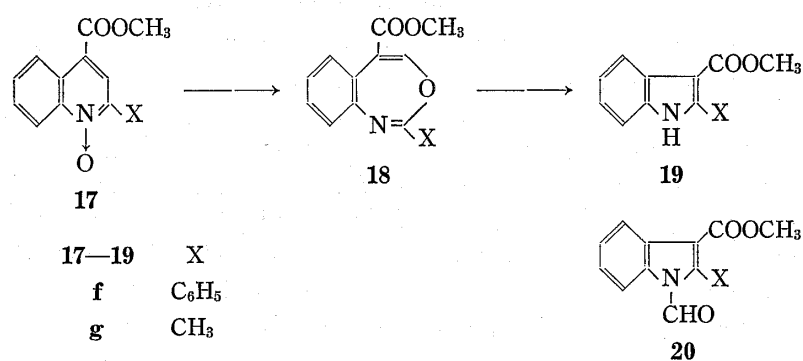
14) The formation of such solvent addition products will be described in detail in the subsequent paper of this series. See C. Kaneko, H. Fujii, S. Kawai, K. Hashida, Y. Karasawa, R. Hayashi, and M. Somei, to be published as Part XXXVI.

15) M. Ishikawa, S. Yamada, H. Hotta, and C. Kaneko, *Chem. Pharm. Bull.*, **14**, 1102 (1966). The effect of the substituents upon the relative ratio of the oxazepine and 2-quinolones has been discussed in detail in reference 1.

16) The electronic properties of an alkoxycarbonyl function are quite similar to those of a carboxyl function. In this case, due to the high solubility of the N-oxides (**17**) in aprotic solvents, we used ether, acetone, dichloromethane, *etc.*, as irradiation solvents. The use of an alcohol for the irradiation of **17** (or the corresponding oxazepines: **18**) resulted in a very facile photochemical Michael addition of alcohols to the oxazepines (**18**) to form the solvent adducts (*e.g.*, **16c**). This kind of photo-Michael addition of an alcohol to **18** proceeded much more rapidly than the photo-ring contraction. See reference **14** and the references cited therein.

was stopped at the point where *ca.* half of the N-oxides (**17f, g**) was consumed, the corresponding oxazepines (**18f, g**) were isolated.[17] Further irradiation of the oxazepines afforded the ring-contraction products (**19f, g**) in nearly quantitative yields. These results indicate the intermediacy of the oxazepine species in these ring-contraction reactions and also that ring contraction is a facile photochemical process in these oxazepines (**17**) at ≥ 300 nm, competing with the conversion of the N-oxides to the oxazepines.

Photolysis of **17g** afforded methyl 1-formyl-2-methylindole-3-carboxylate (**20g**) as a minor product (18.7%), together with the expected methyl 2-methylindole-3-carboxylate (**19g**: 57.8%). The structure of the former product was determined from its spectral data and quantitative conversion to the latter compound (**19g**) upon basic hydrolysis. The mechanism of the formation of **20g** from **17g** (and thus, from **18g**) is not clear at present.

Mechanism of the Ring-contraction Reaction of 3,1-Benzoxazepines to Indole Derivatives: Isolation of the 3H-Indole Intermediate

The formation of the indole derivatives (C) from the oxazepines (A) can be accounted for in terms of the intermediacy of 3H-indole species (B). The formation of the species (B) might occur by a photochemically allowed 1,3-sigmatropic rearrangement of the oxazepine system. In the formation of 3-formylindole derivatives (C-1) from unsubstituted oxazepines, this 3H-indole species (B) would afford the final products by 1,3-hydrogen shift. With a carboxyl function at 3-position in B, decarboxylation would account for the formation of the final products (C-1). Since a protic solvent was employed,[11] this decarboxylation step probably occurs thermally, because many cases are known of similar facile thermal decarboxylation reactions in related β-keto- or -imino-carboxylic acid derivatives.[18] The formation of indoles from the oxazepines having a chlorine atom at the 5-position may be explained by assuming initial homolytic fission (probably photochemical) of the C-Cl bond from the 3H-indole intermediate (B: $R_5=Cl$). The resulting solvent-caged biradical (D) would then afford either

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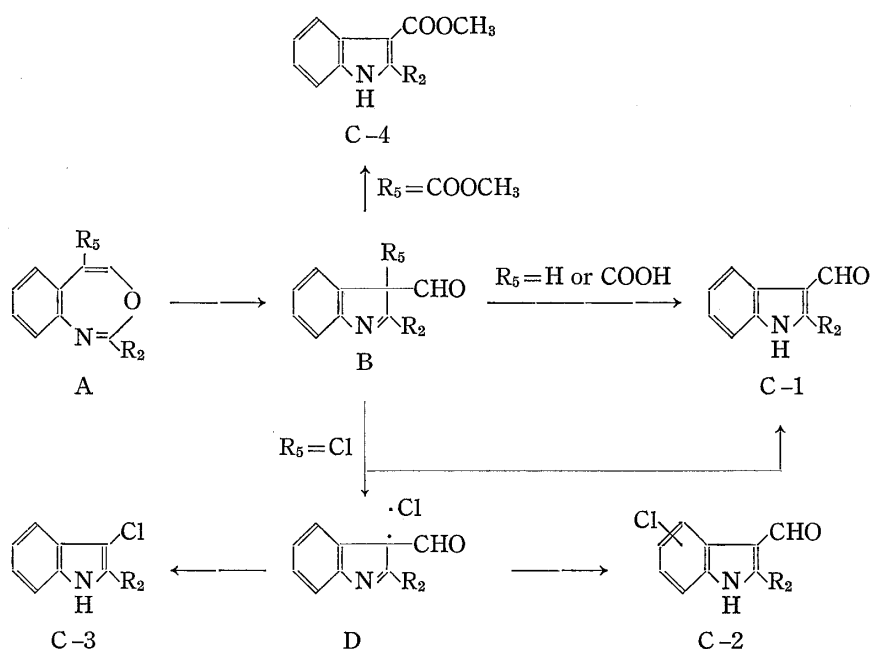
17) Methyl 2-methyl-3,1-benzoxazepine-5-carboxylate (**18g**) too easily solvolyzed to isolate. However, the formation of **18g** was clearly demonstrated by UV and NMR spectroscopy. For example, external irradiation of this N-oxide (**17g**) in CDCl$_3$ in an NMR tube caused the appearance of signals assignable to the oxazepine structure: δ 2.21, s (C$_2$–CH$_3$), 3.76, s (COOCH$_3$), and 7.16, s (C$_4$–H), with concomitant disappearance of those of the N-oxide: δ 2.66, s (C$_2$–CH$_3$), 3.95, s (COOCH$_3$), and 7.90, s (C$_3$–H).

18) R.R. Holmes, K.G. Untch, and H.D. Benson, *J. Org. Chem.*, **26**, 439 (1961).

a mixture of chlorinated indoles as recombination products (C-2), or non-chlorinated 3-formyl-indole (C-1) by hydrogen abstraction from the solvent. In this intermediate, the photo-chemical C-Cl fission seems to be a more facile process than fission of the C-CHO bond, because the yield of 3-chloro-2-cyanoindole (C-3: R_2=CN) was quite low. However, the decarbonyla-tion reaction seems to be the only possible photochemical decomposition process for the 3H-indoles formed from methyl 2-phenyl-3,1-benzoxazepine-5-carboxylate. In accordance with this assumption, methyl 2-phenylindole-3-carboxylate (C-4: R_2=C_6H_5) was obtained from the latter oxazepine by irradiation in an aprotic solvent (*vide supra*).

E

F

Failure to isolate the 3H-indole species (B) in all of the above experiments can be explained by analogy with the mechanism reported by Schaffner *et al.* in terms of the fact that conforma-tionally rigid 'out-of-plane' analogs of α-ary aldehyde[19] (*e.g.*, 3-formyl-3-methylindoline) or the related β,γ-unsaturated aldehyde[20] (*e.g.*, E) undergo ready photochemical decarbonyla-tion with high efficiency (Φ=*ca.* 0.5). They also reported that the system (F), where the formyl group in the above compounds is replaced by an acetyl group, was relatively stable to irradi-ation.[21] Taking this result into consideration and in an attempt to obtain 3H-indole deriva-tives, methyl 4-methyl-2-phenyl-3,1-benzoxazepine-5-carboxylate (22f), which was obtained in 92% yield from methyl 3-methyl-2-phenylquinoline 1-oxide-4-carboxylate (21f) by irradia-tion at $\geq$300 nm (and was stable to this irradiation) was irradiated at 254 nm to afford three stable photo-products (19f, 24f, and 25f). Careful monitoring of the reaction by thin–layer chromatography, however, revealed that a photo-labile product was formed first and that this was converted to these three indoles by prolonged irradiation. Thus, in order to isolate this intermediate, irradiation was stopped when *ca.* half of the oxazepine was consumed. Separation of the products by silica gel column chromatography then afforded the desired compound (23f) in a crystalline form, together with the starting oxazepine and the above three indoles. The photo-labile product (23f) was determined to be methyl 3-acetyl-2-phenyl-3H-indole-3-carboxylate by elemental analysis, mass, and other spectral data. Its UV spectrum [$\lambda_{max}^{CH_3OH}$ nm (log ε): 251 (4.16) and 318 (4.20)] resembled those of 3,3-dialkyl-2-phenyl-3H-indole[22]
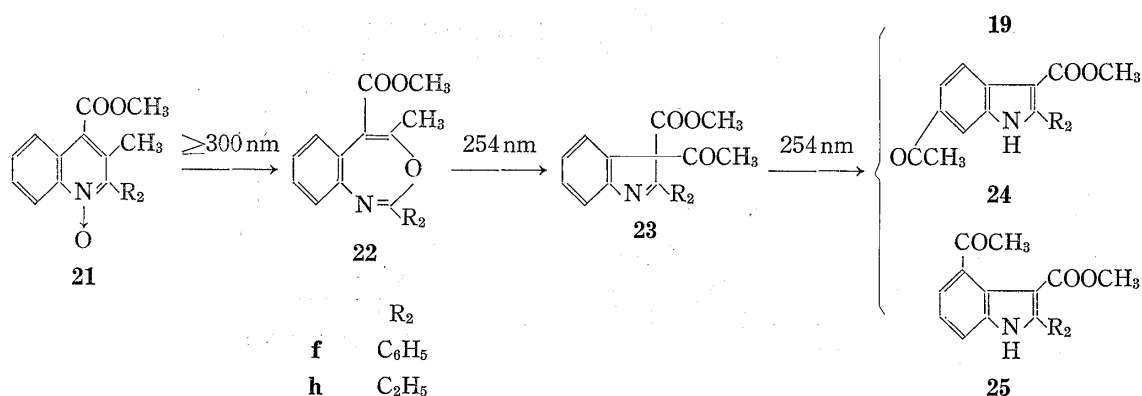

	R_2
f	C_6H_5
h	C_2H_5

Chart 2

19) H. Wolf, H.G. Gonzenbach, K. Muller, and K. Schaffner, *Helv. Chim. Acta*, 55, 2919 (1972).
20) E. Baggiolini, H.P. Hamlov, and K. Schaffner, *J. Am. Chem. Soc.*, 92, 4906 (1970).
21) E. Baggiolini, K. Schaffner, and O. Jeger, *JCS Chem. Commun.*, 1969, 1103.
22) The UV spectra of a series of 3,3-disubstituted 3H-indoles were reported: B. Witkop, J.M. Patrick, and H.M. Kissman, *Chem. Ber.*, 85, 949 (1952).

and its NMR [δ: 1.72 (3H, s), 3.68 (3H, s)] was in accordance with the assigned structure. Furthermore, as expected from a β-diketone-like structure, this indolenine afforded **19f** on heating in methanol (100° in a sealed tube). Actual isolation of the indolenine species (**23f**) confirmed the intermediacy of 3H-indole species (*e.g.*, B) in the photochemical ring contraction of the oxazepines (A) to indoles (C).

Photochemical Reactions of Methyl 3-Acetyl-3H-indole-3-carboxylates and Related Compounds

As mentioned above, irradiation of the oxazepine (**22f**) in acetonitrile at 254 nm until complete consumption of the initially formed photo-labile product (**23f**) afforded, in addition to methyl 2-phenylindole-3-carboxylate (**19f**: 30%), two acetyl derivatives (**24f** and **25f**) in 14 and 12% yields, respectively. Under identical irradiation conditions, these three indoles were also obtained from the indolenine (**23f**) in almost the same ratios as above (41, 15, and 14% respectively). The structures of two acetylated indoles (**24f** and **25f**) were assigned as 6-acetyl- and 4-acetyl-2-phenyl-3-carbomethoxyindoles based on their NMR spectra: **24f** [δ; 2.64 (3H, s), 3.84 (3H, s), 7.82 (H$_5$, dd, J=8.6 and 1.6 Hz), 8.06 (H$_7$, dd, J=1.6 and 0.8 Hz), 8.18 (H$_4$, dd, J=8.6 and 0.8 Hz), 9.22 (NH, b.s)] and **25f** [δ: 2.62 (3H, s), 3.77 (3H, s), 7.15—7.70 (8H, m), 8.84 (NH, b.s)]. The spectrum of the latter compound (**25f**) lacks signals at around δ 8.1 characteristic of H-4 in an alkyl indole-3-carboxylate, and the spectrum of its 1-acetate shows H-7 signals at lower field (δ 8.50, dd, J=8.0 and 1.0 Hz), further supporting the assigned structure. In a similar manner, the corresponding three indoles ((**19h**, **24h**, and **25h**) were obtained from methyl 2-ethyl-3-methylquinoline 1-oxide-4-carboxylate (**21h**).[23]

These reactions seem to be the first example where a carbon unit attached to the 3-position of indolenine species rearranges to either the 4- or 6-position. In order to elucidate the mechanism of these rearrangement reactions, methyl 1-acetyl-2-phenylindole-3-carboxylate (**26**) was irradiated in acetonitrile under the conditions used for **23**. Quite interestingly, in addition to the three expected indoles (**19f**, **24f**, and **25f**), methyl 7-acetyl-2-phenylindole-3-car-
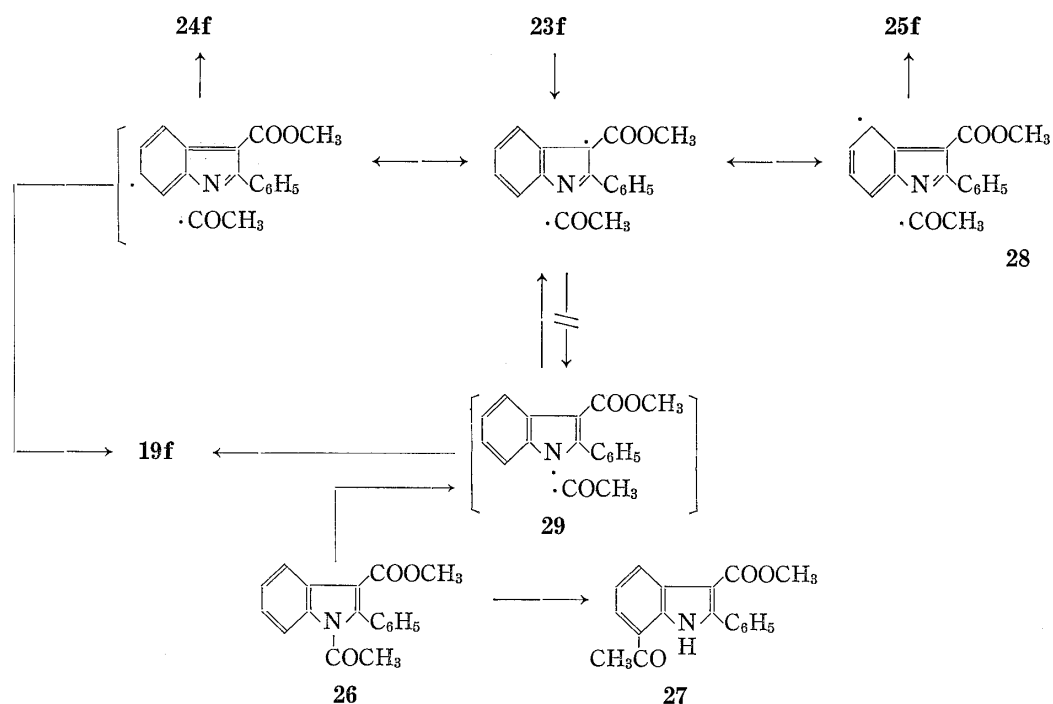

Chart 3

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23) In this case, no attempt was made to isolate the corresponding indolenine intermediate (**23h**).

boxylate (27) was obtained.[24] Taking these results into consideration, the following mechanism can now be proposed for the photo-rearrangement of 23f. A photochemical homolytic fission of the C_3–$COCH_3$ bond in the indolenine (23f) gives the biradical (28) which undergoes either escape of the acetyl group to afford the deacetylation product (19f) or recombination to give 6- and 4-acetylindoles (24f and 25f). An odd electron in the indolyl radical should exists only on C-3, -4, or -6. A radical in which the odd electron exists on the nitrogen atom (e.g., 29) is not included here, because if this were the case, the 7-acetylindole (27) should also be formed from 23f. The absence of the 5-acetyl derivative (30) as a product of photolysis of 26 indicates that the radical (29) may be very unstable and short-lived, rearranging to the more stable radical (e.g., 28). The only other photochemical process that may compete with the above homolytic fission of the N-$COCH_3$ bond in 26 leading to the biradical (29) is a concerted acetyl shift to the 7-position from the 1-position (such a suprafacial 1,3-shift is a photochemically allowed pericyclic reaction[7]) The entire mechanism can thus be formulated as shown in Chart 3.[25]

Solvolytic Ring-contraction Reactions of Methyl 3,1-Benzoxazepine-5-carboxylates

Methyl 3,1-benzoxazepine-5-carboxylates were found to give indoles under solvolytic conditions which were structurally related to the above-mentioned photo-ring contraction products. Thus, for example, heating of methyl 4-methyl-2-phenyl-3,1-benzoxazepine-5-carboxylate (22f) in a sealed tube for 2 hr at 100° afforded, after silica gel chromatography, two ring-contraction products (19f and 23f) in yields of 21 and 23%, respectively, together with recovered starting material (43%). Prolonged heating under these conditions resulted in the almost quantitative formation of methyl 2-phenylindole-3-carboxylate (19f) with the consumption of both the oxazepine and the indolenine (23f). This experiment clearly indicated that thermal conversion of 22f to 19f occurs through 23f. The mechanism for the conversion of the oxazepine (22f) to the indolenine (23f) under solvolytic conditions may be formulated as in Chart 4. The corresponding 2-ethyloxazepine (22h) gave methyl 2-ethylindole-3-carboxylate (19h) on merely standing in methanol at room temperature. The facile solvolysis
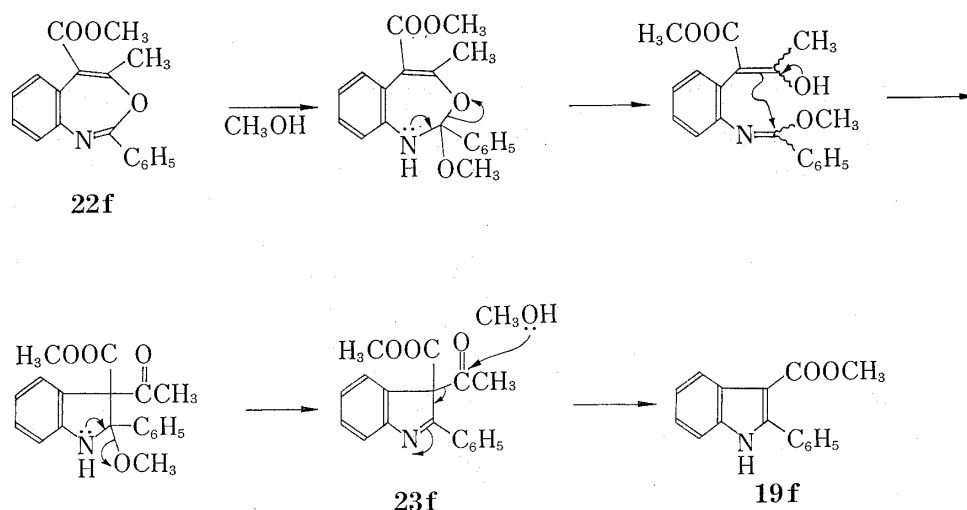
Chart 4

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24) Fries-type photochemical rearrangements of 1-substituted indoles have been reported already, though the indoles examined in these studies had no substituent at the 3-position; a) M. Somei and M. Natsume, *Tetrahedron Lett.*, 1973, 2451; b) S. Naruto and O. Yonemitsu, *Chem. Pharm. Bull.*, 20, 2273 (1972).
25) This mechanism cannot account for the formation of the 5-chloroindole (8) from 5-chloro-2-cyano-3,1-benzoxazepine (5). Further experiments are required to investigate this discrepancy.
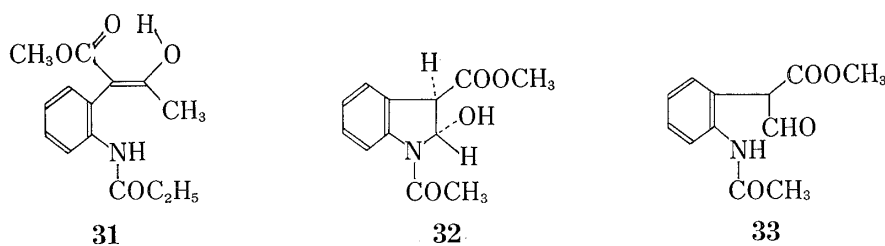
of this oxazepine reflects the instability of the azomethine function in **23h**.[26] Dissolution of the same oxazepine (**22h**) in aqueous acetone at room temperature afforded the ring-opened product (**31**), whose structure was confirmed by elemental analysis and acceptable spectral date. The formation of this product strongly supports the proposed mechanism shown in Chart 4. It should be noted that similar solvolysis of methyl 2-methyl-3,1-benzoxazepine 5-carboxylate (**18g**) gave the 2-indolinol (**32**), instead of giving the ring-opened product (**33**). Clearly, the 4-substituent in the oxazepine system plays a significant role in determining the equilibrium between the ring-opened form and the indolinol form.[27]

Conclusion

In this paper, the photochemical ring contraction of 3,1-benzoxazepines to indole derivatives is described. It was demonstrated that this type of ring-contraction reaction proceeded *via* the 3H- indole intermediate formed probably by $_\pi2_s+_\sigma2_s$ pericyclic reaction of the oxazepine by actual isolation of this intermediate in a crystalline form in the photolysis of methyl 4-methyl-2-phenyl-3,1-benzoxazepine-5-carboxylate (**22f**). Since a wide variety of quinoline 1-oxide can be readily prepared, the present novel photochemical ring-contraction reaction of oxazepines seem to represent a new and general synthetic method for obtaining indole derivatives from quinoline 1-oxides.

Experimental

All melting points were determined in a capillary tube and are uncorrected. IR spectra were determined with a JASCO IRA-2 spectrometer, UV spectra with a Hitachi 323 spectrometer, and NMR spectra with a JEOL JNM-C-60H spectrometer (chemical shifts are in δ-units with coupling constants in Hz, and CDCl$_3$ was used as a solvent unless otherwise stated). For spectroscopic data, the following abbreviations are used: d=doublet, d-d=doublet of doublets, m=multiplet, s=singlet, sh=shoulder, and t=triplet.

Photolyses were carried out in a quartz immersion apparatus equipped with a Toshiba 400P high-pressure mercury lamp with a Pyrex filter (this corresponds to irradiation at ≥300 nm) or without the filter (this corresponds to irradiation at 254 nm) and cooled internally with running water. Irradiation was carried out under argon or nitrogen with stirring.

2-Substituted or 2,3-Disubstituted 4-Carboxyquinolines——These quinolines were synthesized by the so-called Pfitzinger method.[28] Thus, 30 g of isatin and a ketone (1—3 mol equiv. to isatin) in a mixture of 120 ml of aq. 33% KOH and 240 ml of ethanol were refluxed on a water bath for 12—48 hr. The ethanol was evaporated off, followed by neutralization of the residue with acetic acid. The precipitates were collected and washed with water and then with methanol. The products thus obtained were sufficiently pure for subsequent study and were therefore used without further purification. The yields of quinolines were 60-90% based on isatin used. The melting points of these quinolines are listed in Table II.

Methyl 2-Phenyl- and 2-Methylquinoline-4-carboxylate 1-Oxides (17f and 17g)——2-Substituted 4-carboxyquinolines (30.0 g) obtained as described above were heated on a water bath at 90—95° in a mixture of 300 ml of acetic acid and 30 ml of 35% hydrogen peroxide solution. After 4 hr, 30 ml of the peroxide solution was added and the whole was again heated under the same conditions for 3 hr. The precipitates

26) While oxazepines having a phenyl or cyano group at the 2-position are stable, 2-alkyl- or unsubstituted derivatives are readily solvolyzed.[5]

27) Some other examples of substituent effects upon the equilibration in these systems have been summarized. See reference 5c.

28) R.C. Elderfield, "Heterocyclic Compounds," Vol. 4, John Wiley & Sons, New York, 1952, p. 47; W. Pfitzinger, *J. Prakt. Chem.*, [2]33, 100 (1886); *idem, ibid.*, 38, 582 (1888).

that appeared on standing overnight in a refrigerator after the addition of 200 ml of water were collected, washed with water and dried. The amounts of the acid N-oxides obtained were 22—25 g. The methyl esters were then obtained by usual methylation of these acid N-oxides using methanol and conc. sulfuric acid (reflux for 12 hr). The esterification yields were almost quantitative. In a revised procedure, esterification prior to the N-oxidation also afforded the desired products in comparable yields. These esters gave satisfactory elemental analyses and spectra. Their melting points are listed in Table II.

**Methyl 2-Ethyl- and 3-Methyl-2-phenylquinoline-4-carboxylate 1-Oxides (21h and 21f)——2-Ethyl-3-methylquinoline-4-carboxylic acid (3.0 g) was dissolved in a methanolic sodium methoxide solution [prepared by the addition of sodium (0.41 g) to 30 ml of ab. methanol]. After the addition of 1.5 ml of dimethyl sulfate, the whole was refluxed on a water bath for 2 hr. After removal of the solvent, the residue was neutralized by the addition of aq. K$_2$CO$_3$ solution. Extraction with CH$_2$Cl$_2$, drying over MgSO$_4$, concentration and subsequent recrystallization afforded 1.8 g (56.4%) of the methyl ester. N-Oxidation with hydrogen peroxide in acetic acid as above[29] afforded the corresponding N-oxide (21h) in nearly quantitative yield. Methyl 3-methyl-2-phenylquinoline-4-carboxylate and its N-oxide (21f) were synthesized in a similar manner.[30] The melting points of these products are listed in Table II.

**2-Cyano-6-methoxyquinoline 1-Oxide (1b)——6-Methoxyquinoline was oxidized by Ochiai's method (at 70—75°) to give the N-oxide, mp 105.0—106.0° (recrystallized from acetone) in 80% yield. This N-oxide was then treated with KCN in water in the presence of benzoyl chloride (the procedure is essentially the same as Henze's modification of the Reissert reaction[31]) to give 2-cyano-6-methoxyquinoline, mp 126—128° (recrystallized from methanol) in 78% yield. N-Oxidation by Ochiai's method (at 80—85°) afforded the N-oxide (1b), mp 220—221° (recrystallized from CHCl$_3$) in 81% yield. *Anal.* Calcd for C$_{11}$H$_8$N$_2$O$_2$: C, 65.99; H, 4.03; N, 13.99. Found: C, 66.12; H, 4.16; N, 13.78.

**4-Chloro-2-cyanoquinoline 1-Oxide (4)——4-Chloro-2-cyanoquinoline[10] was oxidized by Ochiai's method (at 80—85°) to give the N-oxide (4) in 73% yield, mp 158—160.5° (recrystallized from acetone). *Anal.* Calcd for C$_{10}$H$_5$ClN$_2$O: C, 58.70; H, 2.46; N, 13.69. Found: C, 59.01; H, 2.50; N, 13.56.

3,1-Benzoxazepines——(a) The oxazepines (1a and 1c) were prepared according to the method reported previously.[32]

(b) Syntheses of Crystalline 5-Methoxycarbonyl-, 5-Chloro- and 7-Methoxyoxazepines: These oxazepines were obtained from the corresponding N-oxides by irradiation at ≥300 nm in acetone. The products were separated by silica gel column chromatography using a hexane–ether mixture as an eluting solvent. In most cases, the yields of the deoxygenation products were poor (only 3—10%), while the oxazepines were obtained in 80—90% yield. Prolonged irradiation of methyl 2-phenylquinoline-4-carboxylate-1-oxide (17f) resulted in the formation of a significant amount of the ring-contraction product (19f). The structures of the oxazepines were established from elemental analyses and spectral data. The following experiment was a typical irradiation reaction: 2 g of 4-chloro-2-cyanoquinoline-1-oxide (4) was dissolved in 960 ml of acetone and the whole was irradiated at ≥300 nm until all of the starting N-oxide disappeared (*ca.* 30 min). The residue obtained after removal of the solvent was chromatographed on 50 g of silica gel. Elution with hexane–ether (5: 1 v/v) afforded 1.60 g (80.1%) of the oxazepine (5). UV $\lambda_{max}^{CH_3CN}$ nm (log ε): 241.0 (4.37), 318.5 (3.53); λ_{max}^{MeOH}: 242.0 (4.40), 325.0 (3.58). NMR, δ: 6.50 (1H, s), 7.35—7.60 (3H, m), 7.78 (1H, m). Further elution with hexane–ether (1: 1 v/v) afforded 164 mg (8.9%) of the deoxygenated base (4-chloro-2-cyanoquinoline),[10] mp 106.5—107.0°.

Melting points and analytical data of these oxazepines are listed in Table III.

**Irradiation of 2-Cyano-3,1-benzoxazepine (2a) and Related Compounds (2b and 2c) in Acetonitrile at 254 nm——A solution of 620 mg of 2-cyano-3,1-benzoxazepine (2a) in 900 ml of acetonitrile was irradiated at 254 nm for 3 hr. The residue obtained after removal of the solvent was chromatographed on silica gel. Elution with CH$_2$Cl$_2$ afforded 500 mg (80.6%) of 2-cyanoindole-3-carboxaldehyde (3a), mp 229—230° dec. (recrystallized from acetone). NMR, δ (DMSO-d_6): 7.1—8.25 (4H, m), 9.94 (1H, s, CHO). IR ν_{max}^{KBr} cm^{-1}: 3150, 2220, 1650. *Anal.* Calcd for C$_{10}$H$_6$N$_2$O: C, 70.58; H, 3.55; N, 16.46. Found: C, 70.39; H, 3.63; N, 16.45. On treatment with hydrazines, the monohydrazone [mp 268—270°, MS *m/e*: 184 (M$^+$)] and the phenylhydrazone [mp 204—205°, MS *m/e*: 260 (M$^+$)] were obtained.

In a similar way, two other indole-3-carboxaldehydes (3b, mp 201—202°, and 3c, mp 250—252°) were obtained from the corresponding oxazepines (2b and 2c) in 53—60% yield. The structure of 3c was confirmed to be 2-phenylindole-3-carboxaldehyde by mixed melting point determination with an authentic sample.[8]

29) The N-oxidation of pyridine bases with hydrogen peroxide in acetic acid was discovered by Ochiai and is known as Ochiai's method: E. Ochiai, *J. Org. Chem.*, 18, 534 (1953); *idem*, "Aromatic Amine Oxides," Elsevier, Amsterdam, 1967, p. 24—26.
30) The esterification of 3-substituted quinoline 4-carboxylic acids with methanol in the presence of sulfuric acid afforded only the starting materials.
31) M. Henze, *Chem. Ber.*, 69, 1599 (1936).
32) C. Kaneko and S. Yamada, *Rept. Res. Inst. Med. Engi., Tokyo Medico-Dental Univ.*, 2, 804 (1966); *idem*, *Chem. Pharm. Bull.*, 14, 555 (1966).

TABLE II. Melting Points of 4-Carboxyquinolines, Their N-Oxides,
and the Corresponding Methyl Esters[a]

Substituent	4-Carboxyquinoline			4-Methoxycarbonylquinoline		
	Parent base	N-Oxide		Parent base	N-Oxide	
2-Me	243—244°[b] (dec.)	233—235° (dec.)	(11d)	60—61°[c]	134—135°	(17g)
2-Ph	208—210°[d] (dec.)	260—262° (dec.)	(11c)	54—55°[e]	119—120°	(17f)
2-Ph, 3-Me	296—298°[f] (dec.)	235—238° (dec.)		81—83°	124—125°	(21f)
2-Et, 3-Me	263—265°[g] (dec.)	214—216° (dec.)		71—73°	90— 92°	(21h)

a) The structure of each ester was supported by satisfactory analysis data and by its mass spectrum.
All the acids showed the molecular ions in their mass spectra.
b) W. Pfitzinger, *J. Prakt. Chem.*, [2] **33**, 100 (1886); *idem, ibid.*, **38**, 582 (1888); *idem, ibid.*, **56**, 283
(1897).
c) H. Meyer, *Monatsh. Chem.*, **28**, 51 (1907).
d) W. Pfitzinger, *J. Prakt. Chem.*, **56**, 293 (1897).
e) H. Meyer, *Monatsh. Chem.*, **28**, 39 (1907).
f) J.v. Braun and L. Brauns, *Chem. Ber.*, **60**, 1253 (1927); R.F. Brown *et al.*, *J. Am. Chem. Soc.*,
68, 2705 (1946).
g) C.F. Koelsch, *J. Org. Chem.*, **16**, 1362 (1951).

TABLE III. Crystalline 3,1-Benzoxazepine Derivatives

Substituent (comp.)		mp	Elemental composition	Calcd			Found		
				C	H	N	C	H	N
2-CN 7-OMe	(2b)	133.0—134.0°[a]	$C_{11}H_8N_2O_2$	65.99	4.03	13.99	65.83	4.13	14.02
5-Cl 2-CN	(5)	96.5— 97.0°[b]	$C_{10}H_5ClN_2O$	58.70	2.46	13.69	59.09	2.49	13.68
5-COOMe 2-Ph	(18f)	80.5— 81.5°[b]	$C_{17}H_{13}NO_3$	73.11	4.69	5.02	73.18	4.81	4.92
5-COOMe 4-Me, 2-Ph	(22f)	81.0— 82.0°[b]	$C_{18}H_{15}NO_3$	73.70	5.15	4.78	73.78	5.18	4.65

a) Recrystallized from acetone–CHCl₃.
b) Recrystallized from hexane–ether.

All of these oxazepines were stable to irradiation at ≥300 nm. The photo-induced ring contraction reactions at 254 nm also proceeded in an alcoholic solvent with these oxazepines (2a—2c). The UV spectra of these indole 3-carboxaldehydes were reported in detail in reference 3a.

Irradiation of Methyl 2-Phenyl-3,1-benzoxazepine-5-carboxylate (18f) in an Aprotic Solvent at ≥300 nm ——The oxazepine (18f) was irradiated at ≥300 nm in 880 ml of acetone (other aprotic solvents, such as acetonitrile, were also used) until the starting material disappeared on TLC. Removal of the solvent followed by recrystallization from benzene afforded 661 mg of methyl 2-phenylindole-3-carboxylate[33] (19f). On silica gel column chromatography of the mother liquor, a further crop (628 mg) of 19f was obtained by elution with hexane–ether (7: 1 v/v). The total yield of 19f reached 96.0%. mp 149.5—150.5°. UV λ_{max}^{MeOH} nm (log ε): 242.5 (4.48), 300 (4.20). ν_{max}^{KBr} cm⁻¹ 3300, 1665, 1215. NMR δ: 3.75 (3H, s), 7.06—7.50 (6H, m), 7.66 (2H, m), 8.16 (1H, m), 8.86 (1H, broad s; NH). *Anal.* Calcd for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.27; H, 5.14; N, 5.67.

Irradiation of 5-Chloro-2-cyano-3,1-benzoxazepine (5) in Acetonitrile at 254 nm——The oxazepine (5: 712 mg) in 460 ml of CH₃CN was irradiated at 254 nm for 3 hr. The residue obtained after removal of the solvent was chromatographed on silica gel. Elution with hexane–ether (3: 1 v/v) yielded 44 mg of the oxazepine (5). Elution with hexane–ether (1:1 v/v) and ether alone afforded the following products, 6, 9, 10, 3a, 8, and 7 in yields of 0.7, 1.0, 4.6, 38.8, 2.5, and 6.3%, respectively. The NMR spectral data for these 3-formylindoles are summarized in Table I.

33) U. Straus, H.P. Harter, M. Neuenschwander, and O. Schindler, *Helv. Chim. Acta*, **55**, 771 (1972).

3-Chloro-2-cyanoindole (6). mp 140—144° (recrystallized from ether–hexane). UV λ_{max}^{MeOH} nm (log ε): 227.5 (4.51), 288.0 (4.24), ν_{max}^{KBr} cm^{-1}: 3290, 2220. MS m/e: 215 (M$^+$: C$_9$H$_5$ClN$_2$), 215, 213, 178, 176 (base peak), 141, 114, 89.

6-Chloro-2-cyano-3-formylindole (9). mp 248—250°, dec. (recrystallized from acetone). MS m/e: 243 and 241 (M$^+$), 206, 205, 204 (base peak), 203.

7-Chloro-2-cyano-3-formylindole (10). mp 240—244°, dec. (recrystallized from acetone). UV λ_{max}^{MeOH} nm (log ε): 218.5 (4.55), 246.0 (4.37), 253.5 (4.30), 311.0 (4.10). MS m/e: 243 and 241 (M$^+$), 206, 205, 204 (base peak). Anal. Calcd for C$_{10}$H$_5$ClN$_2$O: C, 58.70; H, 2.46; N, 13.69. Found: C, 59.00; H, 2.33; N, 13.67.

2-Cyano-3-formylindole (3a). mp 229—230°, dec. This was identified by comparison with a sample obtained by the photolysis of 2-cyano-3,1-benzoxazepine (2a).

5-Chloro-2-cyano-3-formylindole (8). mp 230—232°, dec. (recrystallized from acetone–hexane). UV λ_{max}^{MeOH} nm (log ε): 222.0 (4.55), 246.5 (4.23), 313.5 (4.14). MS m/e: 243 and 241 (M$^+$), 206, 205, 204 (base peak), 203, 148, 114. IR ν_{max}^{KBr} cm^{-1}: 3220, 2225, 1652. Anal. Calcd for C$_{10}$H$_5$ClN$_2$O: C, 58.70; H, 2.46; N, 13.69. Found: C, 59.20; H, 2.34; N, 13.37.

4-Chloro-2-cyano-3-formylindole (7). mp 210—212°, dec. (recrystallized from acetone). UV λ_{max}^{MeOH} nm (log ε): 219.5 (4.54), 246.0 (4.27), 313.5 (4.05). IR ν_{max}^{KBr} cm^{-1}: 3220, 2225, 1652. MS m/e: 243 and 241 (M$^+$), 206, 205, 204, 203 (base peak), 176, 148, 114. Anal. Calcd for C$_{10}$H$_5$ClN$_2$O: C, 58.70; H, 2.46; N, 13.69. Found: C, 59.08; H, 2.30; N, 13.73.

Irradiation of Methyl 2-Methylquinoline 1-Oxide-4-carboxylate (17g) in an Aprotic Solvent at $\geq$300 nm

———(a) Direct Formation of Indole Derivatives: A solution of the N-oxide (17g: 1.5 g) in 880 ml of acetone was irradiated at $\geq$300 nm until the initially formed oxazepine (18g) disappeared completely on TLC (3 hr 30 min). It was found that the spot corresponding to the oxazepine (18g, see below) appeared first and then disappeared gradually. Removal of the solvent followed by column chromatography on silica gel (45 g) using hexane–ether (3: 1 v/v) afforded 280 mg (18.7%) of the 1-formylindole (20g), 50 mg (3.6%) of the deoxygenated product, and 755 mg (57.8%) of methyl 2-methylindole-3-carboxylate (19g), mp 198—200° (recrystallized from benzene-acetone). The structure of 19g was confirmed by mixed melting point determination with an authentic sample.[34] The structure of 20g was confirmed by elemental analysis, NMR spectroscopy, and its hydrolysis to 19g in aq. KOH–methanol. 20g, mp 133—135° (recrystallized from acetone). NMR δ: 2.95 (3H, s), 3.96 (3H, s), 7.1—7.5 (3H, m), 8.00 (1H, m), 9.33 (1H, s). IR ν_{max}^{KBr} cm^{-1}: 1700, 1585, 1240. UV $\lambda_{max}^{CH_3CN}$ nm (log ε): 212 (4.49), 232 (4.14), 249 (4.07), 256 (4.07), 283 (3.84), 300 (2.93). MS m/e: 217 (M$^+$), 186, 174, 158. Anal. Calcd for C$_{12}$H$_{11}$NO$_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.28; H, 5.13; N, 6.38.

(b) Identification of Methyl 2-Methyl-3,1-benzoxazepine-5-carboxylate (18g) as a Primary Photo-product: External irradiation of the N-oxide (17g) in CDCl$_3$ in a Pyrex NMR tube with a high-pressure mercury lamp resulted in the disappearance of signals of the N-oxide [e.g., δ: 2.66 (3H, s), 3.95 (3H, s), 7.90 (1H, s)] followed by the appearance of new signals assignable to the oxazepine [δ: 2.21 (3H, s), 3.76 (3H, s), 6.7—8.0 (5H, m)]. TLC of the reaction mixture on a silica gel plate using hexane–ether (3: 1 v/v) showed one main spot whose Rf value was much larger than that of the N-oxide (17g). The UV spectrum of the irradiated solution of 17g in CH$_3$CN showed a maximum at 254 nm with a shoulder at $ca.$ 305 nm. These spectral properties are quite similar to those of methyl 2-phenyl-3,1-benzoxazepine-5-carboxylate (18f). NMR of 18f δ: 3.82 (3H, s), 7.44 (1H, s), 7.1—7.7 (7H, m), 8.08 (2H, m). UV λ_{max}^{MeOH} nm (log ε): 255 (4.43), 314 (3.86).

Irradiation of 4-Carboxyquinoline 1-Oxides (11c—e) in Methanol at $\geq$300 nm

———A solution of 2-methyl-quinoline 1-oxide-4-carboxylic acid (11d: 1.0 g) in 950 ml of methanol was irradiated at $\geq$300 nm until all of the N-oxide was consumed ($ca.$ 40 min). The solid obtained upon removal of the solvent was ground and mixed with 4.0 g of celite, and the whole was packed on top of a silica gel column (45 g). Elution with CH$_2$Cl$_2$ afforded 2-methylindole-3-carboxaldehyde[12] (13d, mp 198—200°) in 37% yield. Elution with CH$_2$Cl$_2$–acetone (9: 1 v/v) afforded 1-methyl-2-quinolone-4-carboxylic acid[35] [15d, mp 241—242°, dec. (recrystallized from methanol)] in 20.4% yield. Finally, elution with CH$_2$Cl$_2$–MeOH (9: 1 v/v) gave 3-methyl-2-quinolone-4-carboxylic acid[36] [14d, mp$\geq$300° (recrystallized from methanol)] in 31.2% yield. Both 2-quinolones showed a common molecular ion at m/e 203 and typical carbostyril absorptions [$\lambda_{max}^{95\% EtOH}$ nm (log ε): 15d: 229.5 (4.51), 275.5 (3.78), 283 (3.78), 331 (3.76) and 14d: 221.0 (4.55), 272.5 (3.89), 324.0 (3.88)]. The position of a methyl group in each product was identified by NMR spectroscopy [δ in DMSO-d_6; 15d: 3.63 (3H, s; CH$_3$), 6.94 (1H, s; H-3), and 14d: 2.12 (3H, s; CH$_3$)].

Under the same irradiation conditions, 2-phenylquinoline 1-oxide-4-carboxylic acid (11c) afforded 2-phenylindole-3-carboxaldehyde,[8] mp 250—252° dec. (recrystallized from benzene) in 59% yield and 3-phenyl-2-quinolone-4-carboxylic acid[13] (14c), mp 292—294° (dec.) in 26.3% yield. The solvent addition

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34) W.B. Whalley, *J. Chem. Soc.*, **1951**, 3229.

35) A. Kaufmann and A. Albertini, *Chem. Ber.*, **42**, 3776 (1909).

36) H. Meyer, *Monatsh. Chem.*, **26**, 1311 (1906).

product[14] (16c), mp 183—185° was also obtained in low yield (7.3%). *Anal.* Calcd for $C_{17}H_{15}NO_4$: C, 68.67; H, 5.08; N, 4.71. Found: C, 68.45; H, 5.12; N, 4.66.

Using the above procedure, 4-carboxyquinoline 1-oxide (11e) afforded 3-formylindole[37] (13e), mp 191—193°, and 2-quinolone-4-carboxylic acid[38] (14e), mp$\geq$300°, in 6.3% and 79.0% yields, respectively.

Irradiation of Methyl 4-Methyl-2-phenyl-3,1-benzoxazepine-5-carboxylate (22f) at 254 nm in Acetonitrile
——A solution of the oxazepine (22f; 300 mg) in 300 ml of CH_3CN was irradiated at 254 nm for 4 hr. At this point, starting material still remained in the irradiation mixture as determined by TLC. Removal of the solvent followed by column chromatography on silica gel afforded the following products. Elution with hexane–ether (3 : 1 v/v) yielded 67.0 mg (22.7%) of the oxazepine (22f) and 25.0 mg (8.3%) of the indolenine (23f). Elution with hexane–ether (1 : 1 v/v) afforded 69.0 mg (26.8%) of methyl 2-phenylindole-3-carboxylate (19f). Elution with hexane–ether (1 : 3 v/v) afforded 36 mg (12.0%) of methyl 6-acetyl-2-phenylindole-3-carboxylate (24f) and 31.0 mg (10.3%) of the isomeric 4-acetyl derivative (25f).

Prolonged irradiation (8 hr) gave three indole (19f, 24f, and 25f) in yields of 39, 14, and 12%, respectively. In this case, neither the starting material nor the indolenine was detected in the reaction mixture.

Methyl 3-acetyl-2-phenyl-3H-indole-3-carboxylate (23f). mp 88.0—89.5° (recrystallized from hexane). UV λ_{max}^{MeOH} nm (log ε): 251 (4.16), 318 (4.20). IR ν_{max}^{KBr} cm^{-1}: 1735, 1705, 1520, 1220. NMR δ: 1.72 (3H, s), 3.68 (3H, s), 7.1—7.8 (7H, m), 7.9—8.1 (2H, m). MS m/e: 293 (M$^+$), 251, 220, 190, 179, 165. *Anal.* Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78. Found: C, 73.64; H, 5.18; N, 4.74. This indolenine was converted to 19f by heating in methanol (100° in a sealed tube, 4 hr) or in methanol at room temperature in the presence of HCl or KOH.

Methyl 6-Acetyl-2-phenylindole-3-carboxylate (24f). mp 194.5—195.5° (recrystallized from hexane–ether). UV λ_{max}^{MeOH} nm (log ε): 220.5 (4.16), 266.5 (4.49), 319.5 (4.28). IR ν_{max}^{KBr} cm^{-1}: 3265, 1690, 1660, 1205. NMR δ: 2.64 (3H, s), 3.84 (3H, s), 7.3—7.75 (5H, m; C_6H_5), 7.82 (1H, d-d, $J=8.6$ and 1.6 Hz; H-5), 8.06 (1H, d-d, $J=1.6$ and 0.8 Hz; H-7), 8.18 (1H, d-d, $J=8.6$ and 0.8 Hz; H-4), and 9.22 (1H, broad s; NH).

Methyl 4-acetyl-2-phenylindole-3-carboxylate (25f). mp 195.5—196.5° (recrystallized from ether). UV λ_{max}^{MeOH} nm (log ε): 238.5 (4.46), 318.0 (4.09). IR ν_{max}^{KBr} cm^{-1}: 3230, 1709, 1655, 1240. NMR δ: 2.62 (3H, s), 3.77 (3H, s), 7.15—7.70 (8H, m), 8.84 (1H, broad s; NH). MS m/e: 293 (M$^+$), 278, 262, 220. The 1-acetate of 25f was obtained from 25f by refluxing in acetic anhydride, followed by recrystallization from hexane–ether. mp 103.0—105.0°. IR ν_{max}^{KBr} cm^{-1}: 1735, 1720, 1678, 1215. NMR δ: 1.95 (3H, s), 2.67 (3H, s), 3.70 (3H, s), 7.44 (1H, t, $J=8.0$ Hz; H-6), 7.48—7.60 (5H, m; C_6H_5), 7.70 (1H, d-d, $J=8.0$ and 1.0 Hz; H-5), and 8.50 (1H, d-d, $J=8.0$ and 1.0 Hz; H-7).

Irradiation of Methyl 2-Ethyl-3-methylquinoline 1-Oxide-4-carboxylate (21h) in an Aprotic Solvent at 254 nm——(a) Identification of the Oxazepine (22h) as the Primary Photo-product: (a-1) The N-oxide (21h; 70 mg) in 0.5 ml of $CDCl_3$ in the presence of TMS was irradiated externally in a Pyrex NMR tube with a 400W high-pressure mercury lamp and the reaction was followed by NMR. Upon irradiation, the signals corresponding to the N-oxide [δ: 1.30, t (3H) and 3.22, q (2H) [$J=7.3$ Hz], 2.47 (s; CH_3), and 4.00 (s; COOCH$_3$)] disappeared gradually and new ones corresponding to the oxazepine appeared [δ: 1.25, t (3H) and 2.33 q (2H) [$J=7.6$ Hz], 2.24 (s, CH_3), and 3.74 (s, COOCH$_3$)]. These signals were unchanged even after prolonged irradiation at $\geq$300 nm.

(a-2) An Attempted Isolation of the Oxazepine (22h): A solution of the N-oxide (21h; 900 mg) in 500 ml of acetone was irradiated at $\geq$300 nm for 30 min. The residue obtained upon removal of the solvent was chromatographed on silica gel (45 g). Elution with hexane–ether (7 : 3 v/v) first afforded 109 mg (12.9%) of the deoxygenated base, followed by 59 mg (7.9%) of methyl 2-ethylindole 3-carboxylate (19h). Elution with ether gave 615 mg (63.7%) of the ring-opened hydration product (31).

Methyl 2-ethylindole 3-carboxylate (19h), mp 72.0—73.0° (recrystallized from hexane). UV λ_{max}^{MeOH} nm: (log ε): 214 (4.55), 228 (4.25), 255 (3.95), 282.5 (4.04), 288 sh (4.07). IR ν_{max}^{KBr} cm^{-1}: 3250, 1660, 1205. MS m/e: 203 (M$^+$), 188, 172, 144. NMR δ: 1.34, (3H, t) and 3.20 (2H, q) [$J=8.0$ Hz], 3.95 (3H, s), 7.1—7.4 (3H, m), 8.10 (1H, m), and 8.52 (1H, broad s; NH). *Anal.* Calcd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.89; H, 6.51; N, 6.76.

The hydration product (31), mp 72.5—75.0° (recrystallized from ether). UV λ_{max}^{MeOH} nm: 242. IR ν_{max}^{KBr} cm^{-1}: 3280, 1650, 1525, 1240. NMR δ: 1.20 (3H, t) and 2.36 (2H, q) [$J=7.8$ Hz], 1.82 (3H, s), 3.71 (3H, s), 7.0—7.5 (3H, m), 8.20 (1H, d, $J=8.0$ Hz), 13.12 (1H, s; OH). MS m/e: 263 (M$^+$), 245, 232, 221, 189, 175, 133.

(b) Irradiation at 254 nm: A solution of the N-oxide (21h; 900 mg) in 500 ml of CH_3CN was irradiated *via* a Pyrex filter until disappearance of the starting N-oxide (25 min). At this point, TLC [silica gel plate; hexane–ether (7 : 3 v/v)] of the irradiation mixture indicated the presence of the oxazepine (Rf: 0.76) and a small amount of the deoxygenated base (Rf: 0.70). The filter was then taken off, and irradiation was continued for 4 hr. Separation of the residue by silica gel column chromatography (45 g) gave, on elution with hexane–ether (3 : 1 v/v), 92 mg (10.9%) of the deoxygenated base and 180 mg (24.1%) of methyl 2-ethylindole-3-carboxylate (19h). Elution with ether afforded first 70 mg (7.8%) of the 6-acetylindole (24h) and then

37) J. Thesing, *Chem. Ber.*, 87, 507 (1954).
38) R.A. Egli and C. Richter, *Helv. Chim. Acta*, 40, 499 (1957).

45 mg (5.9%) of a semisolid fraction corresponding spectrally to the 4-acetylindole (25h).

Methyl 6-acetyl-2-ethylindole-3-carboxylate (24h), mp 159—161° (recrystallized from hexane–ether). UV λ_{max}^{MeOH} nm: 267, 303. IR ν_{max}^{KBr} cm^{-1}: 3380, 1700, 1655, 1290, 1190. NMR δ: 1.38 (t, 3H) and 3.25 (q, 2H) [J=7.8 Hz], 2.67 (3H, s), 3.96 (3H, s), 7.81 (1H, d, J=8.5 Hz; H-5), 8.13 (1H, d, J=8.5 Hz; H-4), 8.09 (1H, s, H-7), and 9.47 (1H, broad s; NH). MS m/e: 245 (M$^+$), 230, 214.

Methyl 4-acetyl-2-ethylindole-3-carboxylate (25h). UV λ_{max}^{MeOH} nm: 220, 260 sh, 290. NMR δ: 1.31 (3H, t) and 3.08 (2H, q) [J=7.8 Hz], 2.56 (3H, s), 3.83 (3H, s), 7.1—7.4 (3H, m), 8.99 (1H, broad s, NH). MS m/e: 245 (M$^+$), 230, 213.

N-Acetylation of Methyl 2-Phenylindole-3-carboxylate (19f)——A solution of 700 mg of methyl 2-phenyl-indole-3-carboxylate (19f) in 30 ml of acetic anhydride was refluxed for 12 hr. After the reaction, the solvent was evaporated off under reduced pressure and the residue was chromatographed on a silica gel column. Elution with hexane–ether (1:1 v/v) afforded first 710 mg (87.0%) of methyl 1-acetyl-2-phenylindole-3-carboxylate (26) and then unchanged 19f (84 mg; 12%).

Methyl 1-acetyl-2-phenylindole-3-carboxylate (26): mp 76.0—78.0° (recrystallized from hexane–ether). UV λ_{max}^{MeOH} nm: 228.0, 253 sh, 300.0; the spectrum after the addition of aq. KOH solution was identical with that of methyl 2-phenylindole-3-carboxylate (19f). IR ν_{max}^{KBr} cm^{-1}: 1702, 1684, 1290, 1235. NMR δ: 1.88 (3H, s), 3.74 (3H, s), 7.2—7.7 (8H, m), 8.1—8.4 (2H, m). MS m/e: 293 (M$^+$).

Irradiation of Methyl 1-Acetyl-2-phenylindole-3-carboxylate (26)——A solution of 286 mg of the 1-acetate (26) in 300 ml of CH$_3$CN was irradiated at 254 nm for 30 min. The residue obtained upon removal of the solvent was chromatographed on silica gel (15 g). Elution with hexane–ether (4:1 v/v) afforded 15.5 mg of the 7-acetylindole (27) and 88.4 mg (36.0%) of the deacetylated indole (19f). Elution with hexane–ether (1:2 v/v) gave 69.1 mg (24.1%) of methyl 6-acetyl-2-phenylindole-3-carboxylate (24f) and 10.2 mg (3.6%) of the 4-acetyl derivative (25f), respectively.

Methyl 7-acetyl-2-phenylindole-3-carboxylate (27), mp 113—114° (recrystallized from hexane–ether). IR ν_{max}^{KBr} cm^{-1}: 3480, 1685, 1645, 1265, 1180. NMR δ: 2.64 (3H, s), 3.77 (3H, s), 7.05—7.80 (7H, m), 8.36 (1H, d, J=7.8 Hz), 10.55 (1H, broad s, NH).

Solvolysis of Methyl 4-Methyl-2-phenyl-3,1-benzoxazepine-5-carboxylate (22f) in Methanol——A solution of 300 mg of the oxazepine (22f) in 10 ml of methanol was heated at 100° in a sealed tube for 2 hr. The residue obtained upon removal of the solvent was chromatographed on silica gel (9 g). Elution with hexane–ether (9:1 v/v) afforded first 130 mg (43.3%) of the unchanged starting material and then 96 mg (32.1%) of the indolenine (23f). Elution with hexane–ether (1:2 v/v) gave 56 mg (21.8%) of methyl 2-phenylindole-3-carboxylate (19f). Prolonged heating (6 hr) resulted in complete disappearance of both the oxazepine and indolenine, and the formation of methyl 2-phenylindole-3-carboxylate (19f) in nearly quantitative yield. Heating of the pure indolenine (23f) under the same conditions also afforded the same indole (19f) in quantitative yield.

Solvolysis of Methyl 2-Phenyl-3,1-benzoxazepine-5-carboxylate (18f) in Methanol——The oxazepine (18f; 100 mg) in 30 ml of methanol was heated for 12 hr in a sealed tube. On removal of the solvent, methyl 2-phenylindole-3-carboxylate (19f) was obtained in quantitative yield.

Solvolysis of Methyl 2-Ethyl-4-methyl-3,1-benzoxazepine-5-carboxylate (22h)——A solution of 632 mg of methyl 2-ethyl-3-methylquinoline 1-oxide-4-carboxylate (21h) in 300 ml of acetone was irradiated at ≥300 nm for 20 min and the reaction mixture was concentrated to exactly 50 ml.

(a) Solvolysis in Methanol: Methanol (20 ml) was added to 10 ml of the above solution and the mixture was kept standing at room temperature for 10 hr. The residue obtained upon removal of the solvent was chromatographed on silica gel (5 g). Elution with hexane–ether (2:1 v/v) gave 12 mg (10.2%) of the deoxygenated base and 84 mg (80.2%) of methyl 2-ethylindole-3-carboxylate (19h).

(b) Solvolysis in Aqueous Acetone: Water (15 ml) was added to 40 ml of the above solution and the mixture was kept standing at room temperature overnight. The aqueous layer obtained upon removal of the acetone was extracted with CH$_2$Cl$_2$ and dried over Na$_2$SO$_4$. The residue obtained upon removal of the solvent was chromatographed on silica gel (15 g). Elution with hexane–CH$_2$Cl$_2$ (1:1 v/v) afforded 53.5 mg (11.3%) of the deoxygenated base and 19.2 mg (4.6%) of the indole (19h). Elution with CH$_2$Cl$_2$–MeOH (99:1 v/v) gave 390 mg (71.8%) of the water addition product (31), which was identical with the hydration product obtained from the oxazepine (22h) on silica gel column chromatography.

Solvolysis of Methyl 2-Methyl-3,1-benzoxazepine-5-carboxylate (18g) in Aqueous Acetone——A solution of 289 mg of 4-methoxycarbonyl-2-methylquinoline 1-oxide (17g) in 300 ml of acetone was irradiated at ≥300 nm for 12 min. After concentration *in vacuo* to ca. 20 ml, 10 ml of water was added and the mixture was kept standing at room temperature overnight. The aqueous layer obtained upon removal of the acetone was extracted with CH$_2$Cl$_2$ and dried over Na$_2$SO$_4$. The residue obtained upon removal of the solvent was chromatographed on silica gel (13 g). Elution with hexane–ether (1:1 v/v) afforded 15 mg (5.6%) of the deoxygenated base and 38 mg (15.0%) of methyl 2-methylindole-3-carboxylate (19g). Elution with hexane–ether (1:2 v/v) gave 225 mg (71.9%) of 1-acetyl-3-methoxycarbonyl-2-indolinol (32). The small coupling constant (1.5 Hz) between H-2 and H-3 in the NMR spectrum indicated a *trans*-configuration between the 2- and 3-substituents.

1-Acetyl-3-methoxycarbonyl-2-indolinol (**32**), mp 97.0—99.0° (recrystallized from hexane–acetone). UV λ_{max}^{MeOH} nm: 247, 278 sh, 285 sh. ν_{max}^{KBr} cm^{-1}: 3300, 1735, 1640, 1260. NMR (in DMSO-d_6) δ: 2.30 (3H, s), 3.64 (3H, s), 4.00 (1H, d, $J=1.5$ Hz), 4.45 (1H, d, $J=7.0$ Hz; the signals disappeared on addition of D$_2$O), 5.92 (1H, d-d, $J=7.0$ and 1.5 Hz; the signals collapsed to a doublet ($J=1.5$ Hz) on addition of D$_2$O), 6.70—7.40 (3H, m), and 7.93 (1H, d, $J=7.0$ Hz). *Anal.* Calcd for C$_{12}$H$_{13}$NO$_4$: C, 61.27; H, 5.57; N, 5.96. Found: C, 61.34; H, 5.60; N, 5.87.