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Studies on Diazepines. XII.[1] Photochemical Synthesis of Novel 1H-1,3-Benzodiazepines from Isoquinoline N-Imides

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Irradiation of the 1-substituted isoquinoline N-acylimides (3), prepared from isoquinolines (**1**) by successive N-amination and acylation, brought about a novel photo-induced two-step rearrangement to form the fully unsaturated 1H-1,3-benzodiazepines (**4**), which were converted into the indole derivative (**10**) by treatment with acids *via* the ring-opened intermediate (**8**) or into (**11**) upon irradiation presumably *via* the tricyclic valence isomer (**14**).

Keywords——photolysis; rearrangement; ring-expansion; isoquinolines; N-imides; 1H-1,3-benzodiazepines; indoles

Since Streith[3] first showed in 1968 that pyridine N-acylimides undergo photo-induced rearrangement to give 1-acyl-1H-1,2-diazepines, the chemistry of the new ring system and the photochemical behavior of aromatic amine N-imides have been widely investigated[4] in connection with those of related N-oxides and oxazepines.[5] We have previously reported the first synthesis of the fully unsaturated 1,2-benzodiazepines[6] and the analogous 1,2-diazepines[7] condensed with aromatic heterocyclic rings such as pyridine, thiophene, furan, and pyrrole from the corresponding quinoline and quinoline-type condensed pyridine N-imides by irradiation. In contrast, isoquinoline N-imides have been shown upon irradiation to undergo N–N fragmentation to the parent isoquinolines, as well as rearrangement into 1-aminoisoquinoline derivatives.[8,9]

We now report the formation of the hitherto unknown fully unsaturated 1,3-benzodiazepines (**4**) by photolysis of the 1-substituted isoquinoline N-imides (**3**).[10] Some reactions of **4** are also described. Of six theoretically possible benzodiazepines, 1,4- and 1,5-benzodiazepines have been most widely investigated owing to their biological activities.[11] The fully unsatu-

1) Part XI: T. Tsuchiya and J. Kurita, *Chem. Pharm. Bull.*, **28**, 1842 (1980).
2) Location: *Kanagawa-machi, Kanazawa 920-11, Japan.*
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5) C. Kaneko, *Yuki Gosei Kagaku Kyokai Shi*, **26**, 758 (1968); G.G. Spence, E.C. Taylor, and O. Buchardt, *Chem. Rev.*, **70**, 231 (1970).
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rated 1,2-[6,12] and 2,3-benzodiazepines[13] have also recently been reported. As for 1,3-diazepines, only two examples of highly substituted monocyclic 1,3-diazepine derivatives are known,[14] whereas, prior to the present work, the 1,3-benzodiazepines were unknown, like the 2,4-benzodiazepines.

The 1-substituted isoquinolines (**1a—d**) were aminated with O-mesitylenesulfonylhydroxylamine (H_2NOMes) according to the method of Tamura *et al.*[8] to give the corresponding N-aminoisoquinolinium mesitylenesulfonates (**2**) in 80—85% yields. Treatment of the salts (**2**) with ethyl chloroformate in the presence of potassium carbonate gave the N-ethoxycarbonylimides (**3a—d**) in good yields. Similarly, treatment of the salt (**2a**) with acylating reagents afforded the corresponding N-acylimides (**3e—g**) as shown in Chart 1.

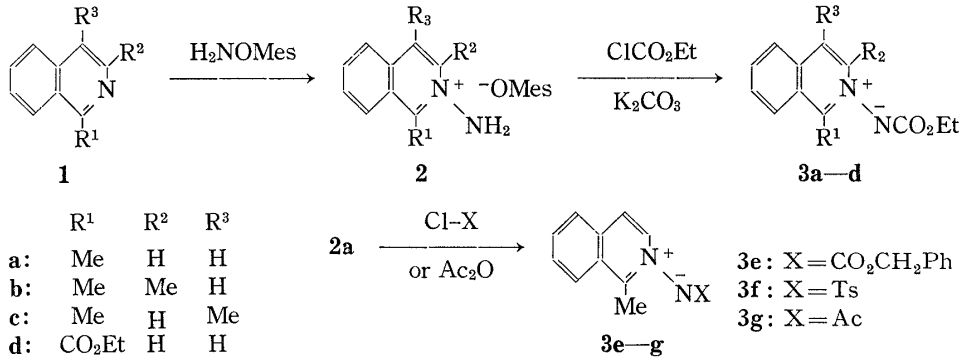

Chart 1

Irradiation of the resulting 1-substituted isoquinoline N-acylimides (**3a—g**) in methylene chloride solution for **1—2** hr gave the corresponding novel 1H-1,3-benzodiazepines (**4**) in the yields shown in Table I, together with the parent isoquinolines (**1**) in 10—30% yields. The 1,3-diazepines (**4**) were found to be very unstable, tending to decompose during the course of the isolation procedure. This instability of the diazepines (**4**) may account for the relatively low yields.

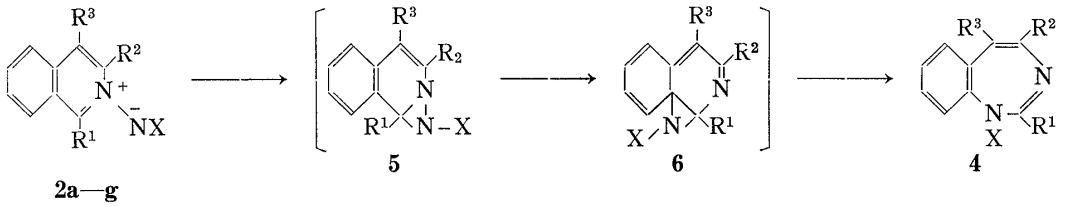

Chart 2

The reaction of **2** to provide **4** may involve an initial rearrangement to the diaziridine intermediate (**5**) analogous to that observed on the photolysis of pyridine and quinoline N-imides,[4,6-9] in which similar diaziridine intermediates are assumed to undergo ring-expansion to give the corresponding 1,2-diazepines and/or N–N bond fission to give 2-amino derivatives. However, in the present photolysis, the diaziridine (**5**) may further rearrange to the aziridine (**6**), followed by ring-expansion to give the new 1,3-diazepines (**4**). In the case of 1-unsubstituted isoquinolines (R^1=H), elimination of the hydrogen atom at C_1 occurs after the cleavage of the N–N bond of the diaziridine intermediates to give the 1-amino derivatives in preference

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Table I. 1,3-Benzodiazepines (4)

Compd. No.	R^1	R^2	R^3	X	Yield[a] (%)	mp[b] (°C)	Formula	Analysis (%) Found (Calcd) C	H	N
4a	Me	H	H	CO_2Et	20	70—71.5	$C_{13}H_{14}N_2O_2$	67.88 (67.81)	6.15 (6.13)	11.96 (12.17)
4b	Me	Me	H	CO_2Et	15	Oil	$C_{14}H_{16}N_2O_2$	68.98 (68.83)	6.52 (6.60)	11.31 (11.47)
4c	Me	H	Me	CO_2Et	20	53—55	$C_{14}H_{16}N_2O_2$	68.78 (68.83)	6.62 (6.60)	11.38 (11.47)
4d	CO_2Et	H	H	CO_2Et	10	96.5—98	$C_{15}H_{16}N_2O_4$	62.61 (62.49)	5.50 (5.59)	9.66 (9.72)
4e	Me	H	H	CO_2CH_2Ph	20	77—78	$C_{18}H_{16}N_2O_2$	73.96 (73.96)	5.53 (5.52)	9.59 (9.58)
4f	Me	H	H	Ts	7	220—221	$C_{17}H_{16}N_2O_2S$	65.44 (65.36)	5.08 (5.16)	8.73 (8.97)
4g	Me	H	H	Ac	30	98—99.5	$C_{12}H_{12}N_2O$	72.28 (71.98)	5.99 (6.04)	13.79 (13.99)

a) Isolation yield.
b) Recrystallized from *n*-hexane–isopropyl ether.

to the second rearrangement into the aziridine (**6**). On the other hand, in the present case ($R^1 \neq H$), the former path can not occur because of the presence of the substituents, and thus the latter predominates. Though this type of reaction involving a two-step rearrangement and ring-expansion to 1,3-oxazepines is very well known in the photolysis of aromatic amine N-oxides,[5] the present result is the first example among aromatic amine N-imides.

The physical and analytical data for the 1,3-diazepines (**4**) are also collected in Table I. The spectral data, summarized in Table II, and the results of the following chemical studies are consistent with the proposed structures, eliminating other possible structures such as 2H- and 3H-2,3-benzodiazepines.

Table II. Spectral Data for the 1,3-Benzodiazepines (4)

Compd. No.	MS *m/e* (M^+)	IR ν_{max}^{KBr} cm^{-1} (C=O)	UV λ_{max}^{EtOH} nm (ε)	NMR δ ($CDCl_3$) $J_{4,5}$=8—9 Hz
4a	230	1710	240(9000) 285(5200)	2.40 (3H, s, 2-Me), 6.44 (1H, d, 5-H), 6.92 (1H, d, 4-H), 7.1—7.5 (4H, m, Ar–H), 1.26 and 4.18 (3H, t, and 2H, q, CO_2Et)
4b	244	1700	244(9100) 285(5700)	2.13 (3H, br, 4-Me), 2.37 (3H, s, 2-Me), 6.27 (1H, br, 5-H), 7.0—7.5 (4H, m, Ar–H), 1.26 and 4.17 (3H, t, and 2H, q, CO_2Et)
4c	244	1700	240(9200) 283(5600)	2.18 (3H, br, 5-Me), 2.34 (3H, s, 2-Me), 6.79 (1H, br, 4-H), 7.1—8.4 (4H, m, Ar–H), 1.25 and 4.16 (3H, t, and 2H, q, CO_2Et)
4d	288	1720	248(16000) 266(sh.)	1.41 and 4.42 (3H, t, and 2H, q, 2-CO_2Et), 6.11 (1H, d, 5-H), 6.62 (1H, d, 4-H), 7.1—7.5 (4H, m, Ar–H), 1.36 and 4.35 (3H, t, and 2H, q, N-CO_2Et)
4e	292	1710	240(9900) 285(5700)	2.40 (3H, s, 2-Me), 6.52 (1H, d, 5-H), 6.99 (1H, d, 4-H), 7.2—7.6 (9H, m, Ar–H), 5.23 (2H, br, $-CH_2-$)
4f	312	—	232(sh.) 259(19900) 275(sh.)	2.39 (3H, s, 2-Me), 6.18 (1H, d, 5-H), 6.47 (1H, d, 4-H), 7.2—7.7 (4H, m, Ar–H), [2.51 (3H, s), 7.2—7.7 (2H, m), 8.09 (2H, m), Ts]
4g	220	1660	240(9400) 284(5400)	2.46 (3H, s, 2-Me), 6.56 (1H, d, 5-H), 7.06 (1H, d, 4-H), 7.2—7.6 (4H, m, Ar–H), 1.80 (3H, s, Ac)

Treatment of the diazepine (**4a**) with methanol or ethanol containing acetic acid resulted in the formation of solvent adducts (**7**), which were decomposed during isolation to give the ring-opened product (**8**) and 2-hydroxy-2,3-dihydroindole derivative (**9**) in 70% and 15% yields, respectively. Treatment of either **8** or **9** with hydrogen chloride gave 1-ethoxycarbonylindole (**10**), which was also directly obtained from the 1,3-diazepine (**4a**) by treatment with hydrogen chloride in methanol. Similarly, the diazepine (**4b**), upon treatment with hydrogen chloride, gave 1-ethoxycarbonyl-2-methylindole (**11**) in high yield. These results indicate that the indole (**10**) may be formed from the ring-opened product (**8**) *via* the dihydroindole (**9**), as observed for 1,3-benzodiazepines.[15]

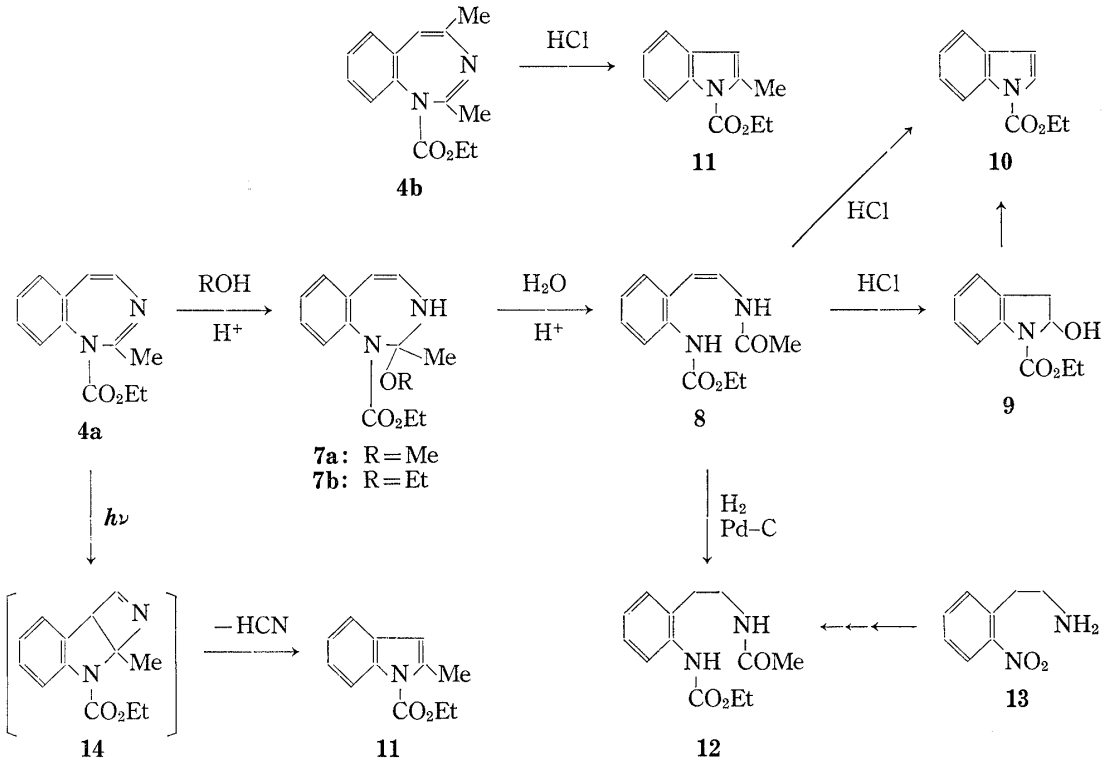

Chart 3

In addition, catalytic hydrogenation of the ring-opened compound (**8**) gave the dihydro compound (**12**), which was identical with an authentic sample prepared from *o*-nitrophenethylamine (**13**) by successive acetylation, reduction, and ethoxycarbonylation.

Finally, further irradiation of the diazepine (**4a**) yielded the 2-methylindole (**11**) in *ca.* 40% yield. Although all attempts to isolate the intermediate (**14**) failed, the formation of the indole (**11**) presumably involves initial cyclization to the tricyclic valence isomer (**14**) followed by extrusion of hydrogen cyanide, analogous to the reaction observed with triazepines.[16] This photochemical behavior of the 1,3-benzodiazepines is also different from that of 1,2-[17] or 2,3-benzodiazepines.[13]

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In conclusion, we present a photochemical synthetic entry into the previously unknown 1H-1,3-benzodiazepines (**4**) class of heterocycles. These compounds are now available for further chemical studies. Attempts to utilize an analogous preparative route to 3H-1,3-benzodiazepines from quinoline N-imides have not been successful to date.

Experimental

Melting points were measured on a Yamato MP-21 apparatus and are uncorrected. Infrared (IR) spectra were determined with a JASCO IRA-2 spectrometer and mass (MS) spectra were recorded on a JEOL D100 instrument. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-MH100 spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard unless otherwise stated; spectral assignments were confirmed by spin-decoupling experiments and, in the case of NH protons, by exchange with D_2O. Microanalyses were performed in the Microanalytical Laboratory of this school by Miss R. Hamano. Photolyses were carried out in an immersion apparatus equipped with a 400 W high-pressure Hg lamp and a Pyrex filter, which was cooled internally with running water.

Materials——1-Methylisoquinoline,[18] 1,3-dimethylisoquinoline,[19] 1,4-dimethylisoquinoline,[20] and 1-ethoxycarbonylisoquinoline[18] were prepared by the reported procedures.

N-Aminoisoquinolinium Mesitylenesulfonates (2a—d)——General Procedure: The procedure of Tamura and co-workers[8] for the preparation of **2a** was employed. A solution of O-mesitylenesulfonylhydroxylamine (1.1 mol eq) in CH_2Cl_2 (100—150 ml) was added dropwise to a solution of the isoquinoline derivatives (**1**: 0.05—0.1 mol) in CH_2Cl_2 (*ca.* 50 ml) with constant stirring in an ice bath. The reaction mixture was stirred for an additional 1 hr. After addition of ether or ethyl acetate (300—500 ml) to the mixture, the resulting crystalline precipitates were collected by filtration and recrystallized from ethanol or ethanol–ethyl acetate to give the salts (**2**). However, in the case of **1c**, the salt (**2c**) could not be crystallized, so the reaction mixture was concentrated *in vacuo* and the residue was used in the following ethoxycarbonylation without isolation.

2a: 84% yield, mp 177—178°, colorless plates (lit.[8] mp 175—176°).

2b: 85% yield, mp 207—208.5°, pale yellow plates. IR ν_{max}^{KBr} cm^{-1}: 3250 (NH). NMR (CD_3OD) δ: 2.19 and 2.55 (3H, s, and 6H, s, Mes–Me), 2.86 (3H, br, 3-Me), 3.30 (3H, s, 1-Me), 6.76 (2H, br, Mes–H), 7.7—8.6 (5H, m, 4-H and Ar–H). *Anal.* Calcd for $C_{20}H_{24}N_2O_3S$: C, 64.49; H, 6.49; N, 7.52. Found: C, 64.52; H, 6.59; N, 7.50.

2d: 80% yield, mp 108.5—110.5°, colorless needles. IR ν_{max}^{KBr} cm^{-1}: 3230 (NH), 1740 (C=O). NMR (CD_3OD) δ: 1.53 and 4.77 (3H, t, and 2H, q, CO_2Et), 2.15 and 2.60 (3H, s, and 6H, s, Mes–Me), 6.79 (2H, s, Mes–H), 8.0—8.2 (4H, m, Ar–H), 8.49 (1H, d, 4-H), 8.71 (1H, d, 3-H), $J_{3,4}$=7 Hz. *Anal.* Calcd for $C_{21}H_{24}N_2O_5S$: C, 60.56; H, 5.81; N, 6.72. Found: C, 60.31; H, 5.90; N, 6.45.

Isoquinoline N-Ethoxycarbonylimides (3a—d)——General Procedure: Solid potassium carbonate (2.3 mol eq) and ethyl chloroformate (*ca.* 1.5—2.0 mol eq) were added to a solution of the salt (**2**: 0.01—0.02 mol) in ethanol (100—200 ml) with stirring. The mixture was stirred for an additional 10—12 hr at room temperature and the resulting precipitate was filtered off. The filtrate was evaporated to dryness *in vacuo* and the residue was extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and evaporated to dryness *in vacuo*. The resulting residue was chromatographed on silica gel using CH_2Cl_2–acetone or acetone as an eluent to give the imides (**3**), which were recrystallized from benzene.

3a: 74% yield, mp 142—143.5°, colorless prisms. IR ν_{max}^{KBr} cm^{-1}: 1615 (C=O). NMR δ: 1.36 and 4.17 (3H, t, and 2H, q, Co_2Et), 3.06 (3H, s, 1-Me), 7.71 (1H, d, 4-H), 7.6—8.2 (4H, m, Ar–H), 8.26 (1H, d, 3-H), $J_{3,4}$=7 Hz. *Anal.* Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.99; H, 6.15; N, 12.03.

3b: 77% yield, mp 95—97°, pale brown plates. IR ν_{max}^{KBr} cm^{-1}: 1620 (C=O). NMR δ: 1.36 and 4.21 (3H, t, and 2H, q, CO_2Et), 2.73 (3H, br, 3-Me), 3.09 (3H, s, 1-Me), 7.4—8.4 (5H, m, 4-H and Ar–H). *Anal.* Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.91; H, 6.55; N, 11.32.

3c: 63% yield (from **1c**), mp 160—162°, pale brown plates. IR ν_{max}^{KBr} cm^{-1}: 1620 (C=O). NMR δ: 1.36 and 4.20 (3H, t, and 2H, q, CO_2Et), 2.64 (3H, br, 4-Me), 3.08 (3H, s, 1-Me), 7.6—8.4 (5H, m, 3-H and Ar–H). *Anal.* Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.76; H, 6.62; N, 11.33.

3d: 83% yield, mp 80—81°, pale yellow prisms. IR ν_{max}^{KBr} cm^{-1}: 1640 (C=O), 1730 (C=O). NMR δ: 1.33 and 4.21 (3H, t, and 2H, q, N–CO_2Et), 1.48 and 4.65 (3H, t, and 2H, q, 1-CO_2Et), 7.7—7.9 (4H, m, Ar–H), 7.97 (1H, d, 4-H), 8.72 (1H, d, 3-H), $J_{3,4}$=7 Hz. *Anal.* Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.13; H, 5.65; N, 9.75.

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1-Methylisoquinoline N-Benzyloxycarbonylimide (3e)——Solid potassium carbonate (2.9 g) and benzyl chloroformate (30—35% in toluene, 9.53 g) were added to a solution of the salt (**2a**: 5 g) in ethanol (150 ml) and the mixture was stirred for *ca.* 10 hr at room temperature. The resulting precipitate was filtered off and the filtrate was evaporated to dryness *in vacuo*. The residue was extracted with CH_2Cl_2 and the extract was dried and evaporated to dryness. The residue was chromatographed on silica gel using CH_2Cl_2–acetone (1: 1) to give the imide (**3e**): 2.64 g, 65% yield, mp 149—150.5°, colorless prisms (from *n*-hexane–benzene). IR ν_{max}^{KBr} cm^{-1}: 1620 (C=O). NMR δ: 3.09 (3H, s, 1-Me), 5.27 (2H, s, $-OCH_2-$), 7.3—8.3 (10H, m, 4-H, Ar–H, and Ph–H), 8.40 (1H, d, 3-H), $J_{3,4}=7$ Hz. *Anal.* Calcd for $C_{18}H_{16}N_2O_2$: C, 73.96; H, 5.52; N, 9.58. Found: C, 74.02; H, 5.54; N, 9.30.

1-Methylisoquinoline N-(*p*-Toluenesulfonyl)imide (3f)——Solid potassium carbonate (850 mg) and *p*-toluenesulfonyl chloride (895 mg) were added to a solution of the salt (**2a**: 1 g, 2.8 mmol) in ethanol (50 ml) and the mixture was stirred for *ca.* 12 hr at room temperature. After removal of the resulting precipitate by filtration, the filtrate was evaporated to dryness *in vacuo*. The residue was extracted with CH_2Cl_2 and the extract was dried, and then evaporated to dryness. The resulting residue was chromatographed on silica gel using CH_2Cl_2–acetone (5: 1) as an eluent to give the imide (**3f**): 694 mg, 79% yield, mp 166—167°, colorless prisms (from ethanol–ethyl acetate). MS *m/e*: 312 (M^+). NMR δ: 2.39 (3H, s, Ts-Me), 3.01 (3H, s, 1-Me), 7.23—7.67 (4H, d, $J=8$ Hz, Ts–H), 7.8—8.4 (4H, m, Ar–H). *Anal.* Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.02; H, 5.74; N, 8.97. Found: C, 65.36; H, 5.56; N, 8.67.

1-Methylisoquinoline N-Acetylimide (3g)——A mixture of the salt (**2a**: 2 g, 5.6 mmol) and acetic anhydride (5 ml) was heated at 80—85° for 5 hr with stirring. After removal of the excess reagent *in vacuo*, the residue was dissolved in CH_2Cl_2 (20 ml) and 50% aq. K_2CO_3 solution (1.5 ml) was added to the solution. After stirring for *ca.* 1 hr at room temperature, the mixture was diluted with CH_2Cl_2 (100 ml), dried over $MgSO_4$, and then evaporated to dryness *in vacuo*. The residue was chromatographed on alumina using CH_2Cl_2–MeOH (50: 1) as an eluent to give the imide (**3g**): 1.06 g, 95% yield, mp 165—166°, colorless needles (from *n*-hexane–benzene). IR ν_{max}^{KBr} cm^{-1}: 1570 (C=O). NMR δ: 2.15 (3H, s, Ac–Me), 3.08 (3H, s, 1-Me), 7.8—8.4 (6H, m, 3-H, 4-H, and Ar–H). *Anal.* Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.76; H, 6.13; N, 13.91.

Photolysis of the N-Imides (3a—g). Formation of 1H-1,3-Benzodiazepines (4a—g)——General Procedure: A solution of the imide (**3**: 0.8—1.0 g) in CH_2Cl_2 (300—350 ml) was irradiated under a nitrogen atmosphere. The photolysis was followed in terms of the disappearance of the spot of the starting material on thin-layer chromatography, and was complete in 1—2 hr. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel using ether–*n*-hexane (2: 1—1: 1) as an eluent to give the 1,3-diazepine (**4**) and the parent isoquinoline (**1**: 10—30% yield) successively. Yields, together with physical and analytical data for **4**, are collected in Table I. Spectral data (MS, IR, UV, and NMR) are also given in Table II.

Treatment of the Diazepine (4a) with Methanol containing Acetic Acid——A mixture of the diazepine (**4a**: 100 mg), abs. methanol (8 ml), and acetic acid (250 mg) was stirred for 2 days at room temperature and was then diluted with CH_2Cl_2 (100 ml). After removal of acetic acid by extraction with satd. $NaHCO_3$, the mixture was washed with satd. NaCl, dried over $MgSO_4$, and evaporated to dryness. The ^1H-NMR spectrum of the resulting residue showed that the residue consisted mainly of the adduct (**7**) [δ: 1.28 and 4.21 (3H, t, and 2H, q, CO_2Et), 2.08 (3H, s, 2-Me), 3.85 (3H, s, 2-OMe), 5.97 (1H, d, 5-H), 6.65 (1H, d, 4-H), 7.0—7.4 (4H, m, Ar–H) $J_{4,5}=9$ Hz]. However, the adduct (**7**) was unstable and decomposed to give the following products. Namely, the residue was chromatographed on silica gel using *n*-hexane–ether (2: 1) as an eluent to give the dihydroindole (**9**) and the ring-opened product (**8**), successively.

8: 75 mg, 70% yield, mp 115—116.5°, colorless prisms (from *n*-hexane–benzene). MS *m/e*: 248 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3300 (NH), 1710 (C=O), 1680 (C=O). NMR δ: 1.31 and 4.18 (3H, t, and 2H, q, CO_2Et), 1.99 (3H, s, Ac–Me), 5.56 (1H, d, $J=9$ Hz, $-C\underline{H}=CH-NH-$), 7.07 (1H, d, $J=9$ Hz, $-CH=C\underline{H}-NH-$), 7.0—7.4 and 7.97 (3H, m, and 1H, d, Ar–H), 6.6 (1H, br, NH), 7.2 (1H, br, NH). *Anal.* Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.81; H, 6.63; N, 11.35.

9: 15 mg, 14% yield, mp 107—108°, colorless prisms (from *n*-hexane–benzene). MS *m/e*: 207 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3425 (OH), 1670 (C=O). NMR δ: 1.40 and 4.35 (3H, t, and 2H, q, CO_2Et), 1.64 (1H, s, OH), 2.97 (1H, dd, $J=13$ and 3 Hz, 3-H), 3.37 (1H, dd, $J=13$ and 7 Hz, 3-H), 5.97 (1H, dd, $J=3$ and 7 Hz, 2-H), 6.9—7.2 (4H, m, Ar–H). *Anal.* Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.85; H, 6.26; N, 6.71.

Treatment of 8 with Hydrogen Chloride——A mixture of **8** (20 mg), methanol (2 ml), and 10% HCl (0.2 ml) was heated at 40—50° for 1 hr. After cooling, the reaction mixture was diluted with CH_2Cl_2 (50 ml) and successively washed with satd. $NaHCO_3$ and satd. NaCl, then dried, and concentrated *in vacuo*. The residue was chromatographed on silica gel using *n*-hexane–ether (10: 1) as an eluent to give N-ethoxycarbonylindole (**10**): 6 mg, 40% yield, colorless oil. MS *m/e*: 189 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (C=O). NMR δ: 1.48 and 4.50 (3H, t, and 2H, q, CO_2Et), 6.60 (1H, d, 3-H), 7.2—8.2 (5H, m, 2-H and Ar–H), $J_{2,3}=4$ Hz. This compound (**10**) was identical with an authentic sample prepared from indole by ethoxycarbonylation with ethyl chloroformate in the presence of *n*-butyl lithium in tetrahydrofuran.[21]

21) S. Kasparek and R.A. Heacock, *Canad. J. Chem.*, **44**, 2805 (1966).

Treatment of 9 with Hydrogen Chloride——A mixture of **9** (35 mg), methanol (3 ml), and 10% HCl (0.3 ml) was heated at 40—50° for 15 min and worked up as described for **8** to give the indole (**10**: 9 mg, 28% yield).

Treatment of the Diazepine (4b) with Hydrogen Chloride——A mixture of **4b** (15 mg), methanol (2 ml), and 10% HCl (0.3 ml) was stirred for 3 hr at room temperature and worked up as described for **8** to give 1-ethoxycarbonyl-2-methylindole (**11**): *ca.* 10 mg, mp 54—55°, colorless prisms (from *n*-hexane–benzene). IR ν_{max}^{KBr} cm^{-1}: 1720 (C=O). NMR δ: 1.42 and 4.36 (3H, t, and 2H, q, CO_2Et), 2.53 (3H, s, 2-Me), 6.17 (1H, s, 3-H), 7.0—8.0 (4H, m, Ar–H). This compound (**11**) was identical with an authentic sample prepared from 2-methylindole by ethoxycarbonylation with ethyl chloroformate in the presence of *n*-butyl lithium.[21]

***o*-Ethoxycarbonylamino-N-acetylphenethylamine (12)**——The compound (**8**: 51 mg, 0.21 mmol) was hydrogenated over 5% Pd–C (100 mg) in methanol (20 ml) with stirring at room temperature under atmospheric pressure. After the uptake of *ca.* 0.2 mmol of hydrogen, the reaction was stopped. The catalyst was filtered off and the filtrate was evaporated to dryness *in vacuo*. The resulting residue was chromatographed on silica gel using CH_2Cl_2–acetone (5: 1) as an eluent to give **12**: 32 mg, 60% yield, mp 109—110°, colorless needles (from *n*-hexane–benzene). MS *m/e*: 250 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3300 and 3450 (NH), 1710 and 1660 (C=O). NMR δ: 1.34 and 4.25 (3H, t, and 2H, q, CO_2Et), 1.96 (3H, s, Ac–Me), 2.8 (2H, m, Ph–CH_2–), 3.3 (2H, m, –$C\underline{H}_2$–NH–), 7.0—7.2 (3H, m, Ar–H), 7.82 (1H, d, Ar–H), 6.4 (1H, br, NH), 7.8 (1H, br, NH). *Anal.* Calcd for $C_{13}H_{18}N_2O_3$: C, 62.38; H, 7.25; N, 11.19. Found: C, 62.65; H, 7.25; N, 10.96. This compound (**12**) was identical with an authentic sample prepared from *o*-nitrophenethylamine by successive acetylation, reduction, and ethoxycarbonylation.

Photolysis of the Diazepine (4a)——A solution of **4a** (31 mg) in CH_2Cl_2 (150 ml) was irradiated under a nitrogen atmosphere for *ca.* 1 hr. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel using *n*-hexane–ether (5: 1) as an eluent to give 1-ethoxycarbonyl-2-methylindole (**11**: *ca.* 10 mg, 37% yield), which was identical with the product obtained from **4b** by treatment with HCl.

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