New Route to 1,3,3a,8a-Tetrahydro-2*H*-benzofuro[2,3-*b*]pyrrol-2-ones from Methyl α-Hydroxy-4*H*-1,2-benzoxazine-4-acetates Obtained by Ring Transformation of 4-Aryl-2-isoxazoline 2-Oxides[1)]

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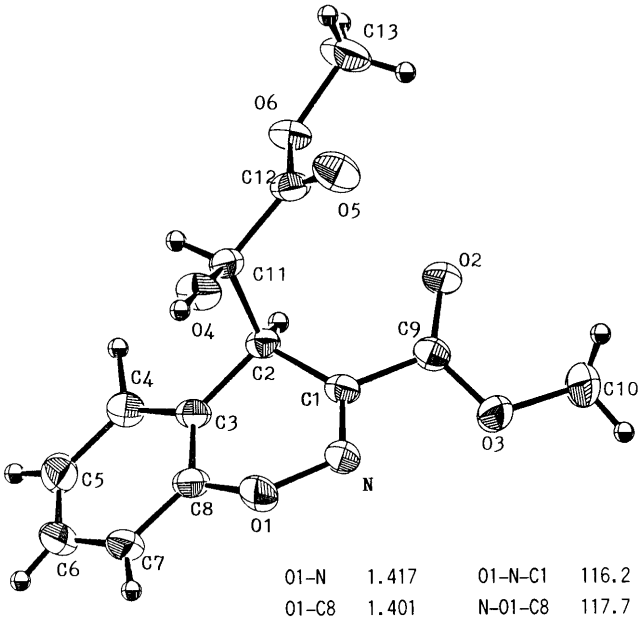
4-Aryl-2-isoxazoline 2-oxides (1) were converted to methyl α-hydroxy-3-methoxycarbonyl-4*H*-1,2-benzoxazine-4-acetates (3) upon treatment with a Lewis acid such as titanium tetrachloride. The structure of 3 was confirmed by X-ray analysis. Tosylates of 3 were treated with triethylamine to yield (*E*)- and (*Z*)-isomers of olefins (5) with (*E*)-preference. Catalytic reduction of each isomer of 5 produced 5,8a-disubstituted 1,3,3a,8a-tetrahydro-2*H*-benzofuro[2,3-*b*]pyrrol-2-ones (6) in moderate yields.

Keywords 2-isoxazoline 2-oxide; 1,2-benzoxazine; benzofuro[2,3-*b*]pyrrole; Lewis acid; ring transformation

A fascinating aspect of heterocyclic chemistry is the ring interconversion of one heterocyclic system into another. This has frequently been used for preparative purposes. In the course of chemical studies of isoxazoline 2-oxides in our laboratory, we encountered a unique ring transformation of 4-(*p*-substituted phenyl)-3,5-bis(methoxycarbonyl)-2-isoxazoline 2-oxides to tricyclic-fused benzofuro[3,3a-*d*]isoxazoles in the presence of a Lewis acid such as $TiCl_4$.[2)] This transformation has been extensively investigated and applied to the synthesis of new heterocyclic ring systems.[3)] In the course of that study, we reported a novel ring transformation of 4-aryl-3,5-bis(methoxycarbonyl)-2-isoxazoline 2-oxides (**1**) into 1-oxido-3*H*-indole 3-acetates (**2**),[4)] as well as conversion of **2** into indole alkaloids.[5)] Although the structure of **2** was elucidated by spectroscopic methods,[4)] reinvestigation of the structure of **2** by single crystal X-ray analysis has now revealed a different structure (**3**) from the previously assigned **2**. Here we wish to give a full account of this ring transformation of **1** and its application to the synthesis of tricyclic alkaloids, tetrahydro-2*H*-benzofuro[2,3-*b*]pyrrol-2-ones, on the basis of the revised structure **3**.

When 3,5-bis(methoxycarbonyl)-4-phenyl-2-isoxazoline 2-oxide (**1a**)[6)] was allowed to react with excess $TiCl_4$, a crystalline product was obtained. The structure of the product was confirmed by means of single crystal X-ray analysis to be methyl α-hydroxy-3-methoxycarbonyl-4*H*-1,2-benzoxazine-4-acetate (**3a**) rather than the previously assigned **2a**. Thus, as can be seen in Fig. 1, **3a** has a 4*H*-1,2-oxazine ring with bond distances ($N–O_1$, 1.417 Å; $O_1–C_8$, 1.401 Å) and intramolecular bond angles ($C_1–N–O_1$, 116.2°; $N–O_1–C_8$, 117.7°), which clearly exclude the originally assigned 3*H*-indole ring. The partial relative stereochemistry at the C_2 and C_{11} asymmetric centers has been elucidated as *R*, *R* or *S*, *S* from the torsion angles ($O_4–C_{11}–C_2–C_3$, 57.9°; $C_3–C_2–C_{11}–C_{12}$, 177.3°). The products from Isoxazoline 2-oxides (**1b—e**) should be similarly represented by **3b—e**, respectively.

The reaction mechanism of this ring transformation may be as follows. The initial electrophilic attack of the Lewis acid causes N–O bond cleavage to give a nitrosonium ion intermediate, which cyclizes through intramolecular aromatic substitution at the *ortho* site by the positively charged oxygen of the nitrosonium species to afford **3** (*cf.* Chart 1). In order to utilize this ring transformation, we investigated various synthetic reactions of **3**, and eventually found a new route to 1,3,3a,8a-tetrahydro-2*H*-benzofuro[2,3-*b*]pyrrol-2-ones (**6**) by a three-step procedure starting from **3** as follows. When compounds **3** were *O*-tosylated with a two-fold molar amount of tosyl chloride, the corresponding 1′-*O*-tosylates (**4**) were obtained in reasonable yields. Subsequent treatment of **4** with an equimolar amount of triethylamine readily yielded the two possible geometric isomers (*E*)-**5** and (*Z*)-**5**, which were separated by silica gel column chromatography. The assignment of the configuration of the isomers was performed on the basis of the ^{1}H-NMR spectra; the H-5 of (*E*)-**5** is strongly deshielded to a lower field (δ 7.8—8.0 ppm) by magnetic anisotropy of the 1′-ester carbonyl group, while the H-5 of (*Z*)-**5** is exceptionally overlapped with other aromatic protons at



O1–N	1.417	O1–N–C1	116.2
O1–C8	1.401	N–O1–C8	117.7
N–C1	1.289	N–C1–C2	127.1

Fig. 1. Molecular Structure of Compound **3a** with the Numbering Scheme Used in the Crystallographic Analysis. Selected Bond Distances (Å) and Bond Angles (°)

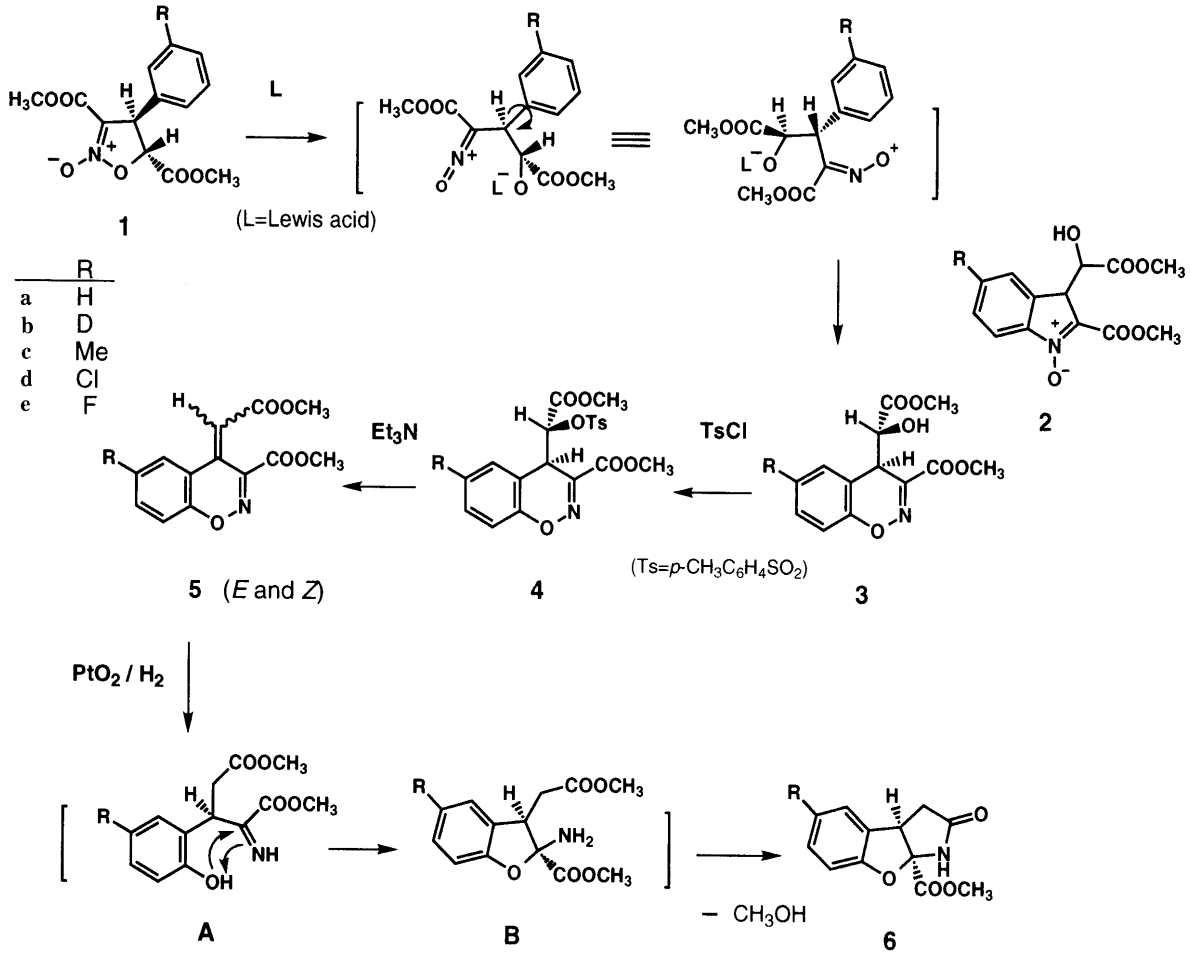
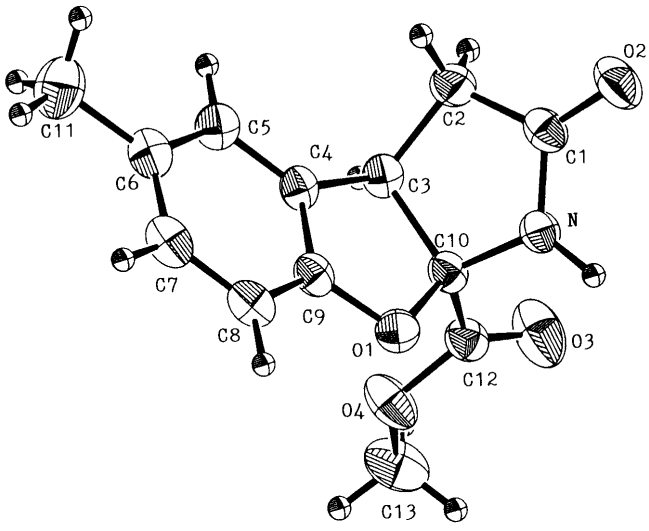


Chart 1

δ 7.0—7.7. Moreover, nuclear Overhauser effect (NOE) experiments showed an increase of 19.4% for the H-5→1′-ester methyl, 22.6% for the H-1′→3-ester methyl of (*E*)-**5d**, and 18.9% for the H-5→H-1′ of (*Z*)-**5d**. This is consistent with the proposed stereochemical relationships. The ratio of *E*:*Z* can be alternatively determined from the signals of the ethylenyl protons (H-1′), *i.e.*, 6.26—6.32 ppm for the (*E*)-isomer, and 6.22—6.24 ppm for the (*Z*)-isomer. The elimination process (**4**→**5**) may proceed mainly by *cis*- rather than *trans*-elimination so that the 4,1′-*erythro*-configuration[4] of **3** should give the (*E*)-olefin in preference to the (*Z*)-olefin.

Finally, reduction of (*E*)- or (*Z*)-**5** was carried out catalytically in acidic media (PtO_2/AcOH). 2*H*-Benzofuro[2,3-*b*]pyrrol-2-ones (**6**) were obtained from (*E*)- or (*Z*)-**5**. The structure of **6** was determined by single crystal X-ray analysis of **6c**. A perspective drawing of **6c** is shown in Fig. 2. The molecule consists of a benzofuro[2,3-*b*] pyrrole ring substituted by a methoxycarbonyl group at C-8a.[7] This transformation may be initiated by reductive ring cleavage of the 1,2-oxazine ring followed by double cyclization to tetrahydrofuran and γ-lactam rings with removal of methanol to afford **6**.

Ring cleavage of the N–O bond in isoxazole or isoxazoline derivatives by acid or base treatment, oxidation, and reduction is a well established method for synthesis of 1,3-difunctional compounds such as β-hydroxy ketones, β-hydroxy oximes, or β-amino alcohols.[8] In contrast, only a few reports deal with the corresponding ring cleavage of 1,2-oxazines leading to 1,4-difunctional compounds, such as 1,4-aminoalcohols and tetrahydro-



N–C1	1.337	O1–C10–N	110.2
N–C10	1.427	N–C1–C2	109.8
C1–C2	1.492	C1–N–C10	115.2

Fig. 2. Molecular Structure of Compound **6c** with the Numbering Scheme Used in the Crystallographic Analysis. Selected Bond Distances (Å) and Bond Angles (°)

pyrroles[9,10] To our knowledge, the above transformation constitutes the first case of one-pot ring closure to a furan ring from a 1,2-oxazine ring. Furthermore, it should be noted that this three-step procedure opens a new route to 8a-substituted benzofuro[2,3-*b*]pyrroles.[11]

Experimental

Melting points were measured with a Yamato MP-1 apparatus and are uncorrected. Spectral data were recorded on the following instruments : Jasco IRA-1 (infrared (IR)), Hitachi 340 (ultraviolet (UV)), JMS D-100 (mass spectrum (MS)), Varian EM-390 (^{1}H-NMR), and JEOL PS-100 (^{13}C-NMR). Tetramethylsilane was used as an internal standard for NMR measurement in chloroform-*d*. Thin-layer chromatography (TLC) was carried out on Kiesel gel 60 (Merck). The developers for TLC were the same as those for column chromatography described below, spots being detected under UV light (254 nm). Column chromatography was done on silica gel (Kanto Kagaku Co., up to 100 mesh) columns.

General Procedure for the Synthesis of Methyl α-Hydroxy-4*H*-1,2-benzoxazine-4-acetates (3a—e) Titanium tetrachloride (0.45 ml, 4 mmol) was added to a solution of a 4-aryl-3,5-bis(methoxycarbonyl)-2-isoxazoline 2-oxide (**1a—e**)[6] (1 mmol), and the mixture was stirred at 0 °C for 0.5 h. After further stirring at room temperature for 0.5 h, the mixture was quenched with aqueous 10% Na_2CO_3 and extracted with dichloromethane (3 × 20 ml). The extract was washed with water (3 × 30 ml), dried over anhydrous Na_2SO_4, and evaporated to dryness *in vacuo*. The residual syrup was applied to a silica gel column and eluted with chloroform–ethyl acetate (4 : 1, v/v) to give the corresponding **3a—e**. The physical and spectral data for **3a**, **3c**, **3d**, and **3e** are given in the previous paper.[4]

Methyl 5,6,7,8-Tetradeuterio-α-hydroxy-3-methoxycarbonyl-4*H*-1,2-benzoxazine-4-acetate (3b) Yield 59%, mp 86—87 °C (ethyl acetate–hexane). IR ν_{max}^{KBr} cm^{-1}: 3430 (OH), 1745 (ester C=O), 1725 (ester C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.02 (1H, m, OH), 3.70 (3H, s, ester Me), 3.92 (3H, s, ester Me), 4.25—4.43 (2H, m, H-4, α). MS *m/z*: 283 (M^+). *Anal.* Calcd for $C_{13}H_9D_4NO_6$: C, 55.12; N, 4.94. Found: C, 55.18; N, 4.98.

General Procedure for the Synthesis of Methyl 6-Substituted 3-Methoxycarbonyl-α-*p*-toluenesulfonyloxy-4*H*-1,2-benzoxazine-4-acetate (4a—d) *p*-Toluenesulfonyl chloride (205 mg, 1.08 mmol) was added to a solution of **3a—d** (0.54 mmol) in 5 ml of pyridine at 0 °C, and the mixture was stirred at 0 °C for 24 h, then partitioned between dichloromethane (20 ml) and H_2O (20 ml). The dichloromethane layer was washed with H_2O (3 × 20 ml), and dried over anhydrous $MgSO_4$. After removal of the solvent, the residue was applied to a silica gel column and eluted with chloroform–ethyl acetate (4 : 1, v/v) to give **4a—d**.

Methyl 3-Methoxycarbonyl-α-*p*-toluenesulfonyloxy-4*H*-1,2-benzoxazine-4-acetate (4a) Yield 80%, mp 146.5—148.5 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1770 (ester C=O), 1735 (ester C=O), 1600 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 2.40 (3H, s, tosyl-Me), 3.63 (3H, s, ester-Me), 3.88 (3H, s, ester-Me), 4.57 (1H, d, $J_{4,\alpha}$=4.0 Hz, H-4), 4.89 (1H, d, $J_{4,\alpha}$=4.0 Hz, H-α), 6.92 (4H, m, H-5,6,7,8), 7.22 (2H, d, J=7.5 Hz, tosyl H-3′,5′), 7.56 (2H, d, J=7.5 Hz, tosyl H-2′,6′). MS *m/z*: 433 (M^+). *Anal.* Calcd for $C_{20}H_{19}NO_8S$: C, 55.42; H, 4.42; N, 3.23; S, 7.40. Found: C, 55.26; H, 4.33; N, 3.25; S, 7.10.

Methyl 5,6,7,8-Tetradeuterio-3-methoxycarbonyl-α-*p*-toluenesulfonyloxy-4*H*-1,2-benzoxazine-4-acetate (4b) Yield 72%, mp 145—146 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1770 (ester C=O), 1730 (ester C=O), 1590 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 2.42 (3H, s, tosyl-Me), 3.66 (3H, s, ester-Me), 3.91 (3H, s, ester-Me), 4.59 (1H, d, $J_{4,\alpha}$=3.0 Hz, H-4), 4.94 (1H, d, $J_{4,\alpha}$=3.0 Hz, H-α), 7.25 (2H, d, J=8.4 Hz, tosyl H-3′,5′), 7.62 (2H, d, J=8.4 Hz, tosyl H-2′,6′). MS *m/z*: 437 (M^+). *Anal.* Calcd for $C_{20}H_{15}D_4NO_8$: C, 54.92; N, 3.46; S, 7.33. Found: C, 55.16; N, 3.25; S, 7.03.

Methyl 3-Methoxycarbonyl-6-methyl-α-*p*-toluenesulfonyloxy-4*H*-1,2-benzoxazine-4-acetate (4c) Yield 60%, mp 120.5—121.5 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1760 (ester C=O), 1730 (ester C=O), 1600 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 2.26 (3H, s, 6-Me), 2.42 (3H, s, tosyl-Me), 3.68 (3H, s, ester-Me), 3.89 (3H, s, ester-Me), 4.55 (1H, d, $J_{4,\alpha}$=2.0 Hz, H-4), 4.85 (1H, dd, $J_{4,\alpha}$=2.0 Hz, H-α), 6.8—7.1 (3H, m, H-5,7,8), 7.18 (2H, d, J=7.8 Hz, tosyl H-3′,5′), 7.53 (2H, d, J=7.8 Hz, tosyl H-2′,6′). MS *m/z*: 447 (M^+). *Anal.* Calcd for $C_{21}H_{21}NO_8S$: C, 56.37; H, 4.73; N, 3.13; S, 7.16. Found: C, 56.30; H, 4.79; N, 3.11; S, 7.00.

Methyl 6-Chloro-3-methoxycarbonyl-α-*p*-toluenesulfonyloxy-4*H*-1,2-benzoxazine-4-acetate (4d) Yield 44%, mp 141—142 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1750 (ester C=O), 1725 (ester C=O), 1620 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 2.43 (3H, tosyl-Me), 3.69 (3H, s, ester-Me), 3.89 (3H, s, ester-Me), 4.54 (1H, d, $J_{4,\alpha}$=3.3 Hz, H-4), 4.82 (1H, d, $J_{4,\alpha}$=3.3 Hz, H-α), 6.9—7.3 (3H, m, H-5,7,8), 7.22 (2H, d, J=9.0 Hz, tosyl H-3′,5′), 7.55 (2H, d, J=9.0 Hz, tosyl H-2′,6′). MS *m/z*: 467 (M^+). *Anal.* Calcd for $C_{20}H_{18}ClNO_8S$: C, 51.34; H, 3.88; Cl, 7.58; N, 2.99; S, 6.85. Found: C, 51.54; H, 3.82; Cl, 7.83; N, 3.08; S, 6.77.

Methyl 6-Fluoro-3-methoxycarbonyl-α-*p*-toluenesulfonyloxy-4*H*-1,2-benzoxazine-4-acetate (4e) Reaction of **3e** with tosyl chloride by the general conditions described above afforded a mixture of **4e** (16%) and the β-eliminated product **5e** (58%, E:Z=3:2). **4e**: mp 157 °C (dec., chloroform–ether). IR ν_{max}^{KBr} cm^{-1}: 1770 (ester C=O), 1730 (ester C=O), 1615 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 2.42 (3H, s, tosyl-Me), 3.67 (3H, s, ester-Me), 3.90 (3H, s, ester-Me), 4.55 (1H, d, $J_{4,\alpha}$=3.4 Hz, H-4), 4.90 (1H, d, $J_{4,\alpha}$=3.4 Hz, H-α), 6.9—7.1 (3H, m, H-5,7,8), 7.23 (2H, d, J=8.5 Hz, tosyl H-3′,5′), 7.60 (2H, d, J=8.5 Hz, tosyl H-2′,6′). MS *m/z*: 451 (M^+). *Anal.* Calcd for $C_{20}H_{18}FNO_8S$: C, 53.21; H, 4.02; N, 3.10; S, 7.10. Found: C, 53.19 ; H, 4.00; N, 3.11; S, 6.84.

General Procedure for the Synthesis of (*E*)- or (*Z*)-Methyl 6-Substituted-3-methoxycarbonyl-4*H*-1,2-benzoxazine-$\Delta^{4,\alpha}$-acetates (5a—e) Triethylamine (0.16 ml, 1.15 mmol) was added to a solution of **4a—e** (1.15 mmol) in 10 ml of dichloromethane, and the mixture was stirred at room temperature for 4 h, then partitioned between dichloromethane (40 ml) and H_2O (50 ml). The dichloromethane layer was washed with H_2O (3 × 20 ml), and dried over anhydrous $MgSO_4$. After removal of the solvent, the residue was applied to the silica gel column and eluted with chloroform to give (*E*)- and (*Z*)-**5a—e**.

(*E*)- and (*Z*)-Methyl 3-Methoxycarbonyl-4*H*-1,2-benzoxazine-$\Delta^{4,\alpha}$-acetate (5a) (*E*)-**5a**: Yield 76%, mp 90.0—90.5 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1730 (ester C=O), 1725 (ester C=O), 1620 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 3.75 (3H, s, ester-Me), 3.95 (3H, s, ester-Me), 6.26 (1H, s, H-1′), 6.8—7.6 (3H, m, H-6,7,8), 8.01 (1H, dd, J=9.0, 2.0 Hz, H-5). MS *m/z*: 261 (M^+). *Anal.* Calcd for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.65; H, 4.16; N, 5.28.

(*Z*)-**5a**: Yield 23%, mp 83.5—84.5 °C (methanol–H_2O). IR ν_{max}^{KBr} cm^{-1}: 1740 (ester C=O), 1705 (ester C=O), 1615 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 3.72 (3H, s, ester-Me), 3.91 (3H, s, ester-Me), 6.22 (1H, s, H-1′), 7.1—7.7 (4H, m, H-5,6,7,8). MS *m/z*: 261 (M^+). *Anal.* Calcd for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.72; H, 4.28; N, 5.11.

(*E*)- and (*Z*)-Methyl 5,6,7,8-Tetradeuterio-3-methoxycarbonyl-4*H*-1,2-benzoxazine-$\Delta^{4,\alpha}$-acetate (5b) (*E*)- and (*Z*)-**5b** were obtained as a mixture. Yield 67% (E:Z=14:1), mp 70—71 °C (from MeOH), pale yellow crystals. IR ν_{max}^{KBr} cm^{-1}: 1735, 1725 (ester C=O), 1705 (ester C=O), 1620 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 3.75, 3.78 (3H, s, ester-Me), 3.94, 3.98 (3H, s, ester-Me), 6.30, 6.25 (1H, s, H-1′).

(*E*)- and (*Z*)-Methyl 3-Methoxycarbonyl-6-methyl-4*H*-1,2-benzoxazine-$\Delta^{4,\alpha}$-acetate (5c) (*E*)-**5c**: Yield 54%, mp 87.0—88.0 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1730 (ester C=O), 1715 (ester C=O), 1610 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 2.37 (3H, s, 6-Me), 3.77 (3H, s, ester-Me), 3.96 (3H, s, ester-Me), 6.27 (1H, s, H-1′), 7.0—7.4 (2H, m, H-7,8), 7.79 (1H, dd, J=9.0, 2.0 Hz, H-5). MS *m/z*: 275 (M^+). *Anal.* Calcd for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 60.82; H, 4.75; N, 5.06.

(*Z*)-**5c**: Yield 32%, mp 76.0—78.0 °C (methanol–H_2O). IR ν_{max}^{KBr} cm^{-1}: 1730 (ester C=O), 1695 (ester C=O), 1610 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 2.38 (3H, s, 5-Me), 3.74 (3H, s, ester-Me), 3.92 (3H, s, ester-Me), 6.22 (1H, s, H-1′), 7.0—7.5 (3H, m, H-5,7,8). MS *m/z*: 275 (M^+). *Anal.* Calcd for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 60.82; H, 4.75; N, 5.06.

(*E*)- and (*Z*)-Methyl 6-Chloro-3-methoxycarbonyl-4*H*-1,2-benzoxazine-$\Delta^{4,\alpha}$-acetate (5d) (*E*)-**5d**: Yield 87%, mp 158—160 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1720 (ester C=O), 1710 (ester C=O), 1615 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 3.80 (3H, s, ester-Me), 3.97 (3H, s, ester-Me), 6.32 (1H, s, H-1′), 7.16 (1H, d, J=9.0 Hz, H-8), 7.43 (1H, dd, J=9.0, 2.4 Hz, H-7), 8.13 (1H, d, J=2.4 Hz, H-5). MS *m/z*: 297 (M^+). *Anal.* Calcd for $C_{13}H_{10}ClNO_5$: C, 52.81; H, 3.41; Cl, 11.99; N, 4.74. Found: C, 52.81; H, 3.35; Cl, 11.76; N, 4.61.

(*Z*)-**5d**: Yield 11%, mp 138—139 °C (methanol). IR ν_{max}^{KBr} cm^{-1}: 1725 (ester C=O), 1700 (ester C=O), 1610 (ester C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.76 (3H, s, ester-Me), 3.93 (3H, s, ester-Me), 6.24 (1H, s, H-1′), 7.19 (1H, d, J=9.0 Hz, H-8), 7.44 (1H, dd, J=9.0, 2.4 Hz, H-7), 7.58 (1H,

d, J=2.4 Hz, H-5). MS m/z: 297 (M^+). *Anal.* Calcd for $C_{13}H_{10}ClNO_5$: C, 52.81; H, 3.41; Cl, 11.99; N, 4.74. Found: C, 52.57; H, 3.31; Cl, 12.11; N, 4.80.

(*E*)- and (*Z*)-6-Fluoro-3-methoxycarbonyl-4*H*-1,2-oxazine-$\Delta^{4,\alpha}$-acetate (5e) (*E*)-**5e**: Yield 86% (from the reaction of **4e** with triethylamine in dichloromethane), mp 123—124 °C (ethanol). IR ν_{max}^{KBr} cm^{-1}: 1730 (ester C=O), 1710 (ester C=O), 1620 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 3.81 (3H, s, ester-Me), 3.98 (3H, s, ester-Me), 6.35 (1H, s, H-1'), 7.2—7.3 (2H, m, H-7,8), 7.93 (1H, td, J=1.2, 2.1, 9.5 Hz, H-5). MS m/z: 279 (M^+). *Anal.* Calcd for $C_{13}H_{10}FNO_5$: C, 55.92; H, 3.61; N, 5.02. Found: C, 56.12; H, 3.57; N, 4.91.

(*Z*)-**5e**: Yield 11% (from the reaction of **4e** with triethylamine in dichloromethane), mp 134—135 °C (ethanol). IR ν_{max}^{KBr} cm^{-1}: 1735 (ester C=O), 1715 (ester C=O), 1610 (C=N). ^{1}H-NMR ($CDCl_3$) δ: 3.76 (3H, s, ester-Me), 3.93 (3H, s, ester-Me), 6.22 (1H, s, H-1'), 7.2—7.3 (3H, m, H-5,7,8), MS m/z: 279 (M^+). *Anal.* Calcd for $C_{13}H_{10}FNO_5$: C, 55.92; H, 3.61; N, 5.02. Found: C, 56.02; H, 3.60; N, 4.92.

General Procedure for the Synthesis of 1,3,3a,8a-Tetrahydro-2*H*-benzofuro[2,3-*b*]pyrrol-2-ones (6a—d) PtO_2 (20 mg) was added to a solution of (*E*)- or (*Z*)-**5** (1.0 mmol) in 10 ml of acetic acid, and the mixture was hydrogenated under H_2 (2 atom, 202630 Pa) for 2 h. The catalyst was filtered off, and the filtrate was concentrated to dryness. The residue was applied to a silica gel column and eluted with chloroform–ethyl acetate (4 : 1) to give **6a—d**.

8a-Methoxycarbonyl-1,3,3a,8a-tetrahydro-2*H*-benzofuro[2,3-*b*]pyrrol-2-one (6a) 58% from (*E*)-**5a**, 55% from (*Z*)-**5a**, mp 145—146 °C (chloroform–hexane). IR ν_{max}^{KBr} cm^{-1}: 3200 (NH), 1750 (ester C=O), 1710 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.56 (1H, dd, $J_{3,3'}$=17.4 Hz, $J_{3,3a}$=3.0 Hz, H-3), 3.00 (1H, dd, $J_{3,3'}$=17.4 Hz, $J_{3',3a}$=9.3 Hz, H-3'), 3.86 (3H, s, ester-Me), 4.41 (1H, dd, $J_{3a,3}$=3.0 Hz, $J_{3a,3'}$=9.3 Hz, H-3a), 6.78—7.37 (4H, m, H-4,5,6,7), 7.13 (1H, m, NH, exchangeable with D_2O). MS m/z: 233 (M^+). *Anal.* Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 61.48; H, 4.64; N, 6.02.

4,5,6,7-Tetradeuterio-8a-methoxycarbonyl-1,3,3a,8a-tetrahydro-2*H*-benzofuro[2,3-*b*]pyrrol-2-one (6b) Yield 56%, mp 149–151 °C (chloroform–hexane). IR ν_{max}^{KBr} cm^{-1}: 3190 and 3100 (NH), 1755 (ester C=O), 1705 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.58 (1H, dd, $J_{3,3'}$=17.7 Hz, $J_{3,3a}$=3.0 Hz, H-3), 3.00 (1H, dd, $J_{3,3'}$=17.7 Hz, $J_{3',3a}$=9.3 Hz, H-3'), 3.86 (3H, s, ester-Me), 4.42 (1H, dd, $J_{3a,3}$=3.0 Hz, $J_{3a,3'}$=9.3 Hz, H-3), 7.05 (1H, br s, NH, exchangeable with D_2O). MS m/z: 237 (M^+). *Anal.* Calcd for $C_{12}H_7D_4NO_4$: C, 60.75; N, 5.90. Found: C,61.04; N, 5.72.

8a-Methoxycarbonyl-5-methyl-1,3,3a,8a-tetrahydro-2*H*-benzofuro-[2,3-*b*]pyrrol-2-one (6c) Yield 44%, mp 204—205 °C (chloroform–hexane). IR ν_{max}^{KBr} cm^{-1}: 3200 and 3090 (NH), 1755 (ester C=O), 1710 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.22 (3H, s, 5-Me), 2.55 (1H, dd, $J_{3,3'}$= 17.6 Hz, $J_{3,3a}$=3.0 Hz, H-3), 3.00 (1H, dd, $J_{3,3'}$=17.6 Hz, $J_{3',3a}$=9.0 Hz, H-3'), 3.86 (3H, s, ester-Me), 4.41 (1H, dd, $J_{3a,3}$=3.0 Hz, $J_{3a,3'}$=9.0 Hz, H-3a), 6.8—7.1 (3H, m, H-4,6,7). MS m/z: 247 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.09. Found: C, 62.67; H, 5.28; N, 5.54.

5-Chloro-8a-methoxycarbonyl-1,3,3a,8a-tetrahydro-2*H*-benzofuro-[2,3-*b*]pyrrol-2-one (6d) Yield 45%, mp 170.5–171 °C (chloroform–hexane). IR ν_{max}^{KBr} cm^{-1}: 3180 and 3100 (NH), 1755 (ester C=O), 1715 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.57 (1H, dd, $J_{3,3'}$=17.7 Hz, $J_{3,3a}$= 3.3 Hz, H-3), 3.00 (1H, dd, $J_{3,3'}$=17.7 Hz, $J_{3',3a}$=9.6 Hz, H-3'), 3.87 (3H, s, ester-Me), 4.40 (1H, dd, $J_{3a,3}$=3.3 Hz, $J_{3a,3'}$=9.6 Hz, H-3a), 7.2—7.4 (3H, m, H-4,6,7). MS m/z: 267 and 269 (M^+). *Anal.* Calcd for $C_{12}H_{10}ClNO_4$: C, 53.85; H, 3.77; Cl, 13.25, N, 5.23. Found: C, 53.87; H, 3.74; Cl, 13.54; N, 5.42.

5-Fluoro-8a-methoxycarbonyl-1,3,3a,8a-tetrahydro-2*H*-benzofuro-[2,3-*b*]pyrrol-2-one (6e) Yield 50%, mp 177—179 °C (chloroform–hexane). IR ν_{max}^{KBr} cm^{-1}: 3150 and 3070 (NH), 1760 (ester C=O), 1700 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.55 (1H, dd, $J_{3,3'}$=18.0 Hz, $J_{3,3a}$= 3.0 Hz, H-3), 3.00 (1H, dd, $J_{3,3a}$=9.5 Hz, $J_{3,3'}$=18.0 Hz, H-3'), 3.88 (3H, s, ester Me), 4.43 (1H, dd, $J_{3a,3}$=3.0 Hz, $J_{3a,3'}$=9.5 Hz, H-3a), 6.7—7.0 (3H, m, H-4,6,7). MS m/z: 251 (M^+). *Anal.* Calcd for $C_{12}H_{10}FNO_4$: C, 57.37; H, 4.01; N, 5.58. Found: C, 56.98; H, 3.96; N, 5.43.

X-Ray Analysis of 3a and 6c A crystal was mounted on a Rigaku AFC-5R diffractometer, and the cell parameters and the intensity data were measured with graphite-monochromated CuK_α (λ=1.54179 Å) radiation at 23 °C. Approximate atomic coordinates were obtained by the direct method using MITHRIL.[12] The parameters of non-hydrogen atoms were refined by the full-matrix least-squares method with anisotropic temperature factors. The hydrogen atoms were located from a difference Fourier synthesis, and refined with isotropic temperature factors. The crystal data are as follows.

3a: Chemical formula $C_{13}H_{13}NO_6$; M.W. 279.25; monoclinic; space group $P2_1/n$; Z=4; unit cell dimensions a=8.584(2) Å, b=19.259(5) Å, c=8.752(2) Å, β=115.81(1)°, V=1302(1) Å^3; D_{cal}=1.424 g cm^{-3}; μ(Cu-K_α)=9.29 cm^{-1}; crystal size 0.3×0.3×0.4 mm. Of the total of 2609 reflections up to the 2θ range of 140.3° (unique reflections, 2450), 1538 were measured as above the 3σ (I) level and were used. The final R value was 0.072

6c: Chemical formula $C_{13}H_{13}NO_4$; M.W. 247.25; monoclinic; space group $P2_1/c$; Z=4; unit cell dimensions a=9.171(2) Å, b=7.209(2) Å, c=18.169(2) Å, β=91.65(2)°, V=1200.6(6) Å^3; D_{cal}=1.368 g cm^{-3}; μ(CuK_α)=8.13 cm^{-1}; crystal size 0.3×0.4×0.5 mm. Of the total of 2624 reflections up to the 2θ range of 140.1° (unique reflections: 2469), 1791 were measured as above the 3σ (I) level and were used. The final R value was 0.059.

The positional parameters for **3a** and **6c** are listed in Tables I and II, respectively.

TABLE I. Positional Parameters and Equivalent Isotropic Thermal Parameters of **3a** with Their Estimated Standard Deviations in Parentheses

Atom	x	y	z	B_{eq}
O_1	0.2830 (6)	−0.1798 (2)	0.9340 (5)	3.7 (2)
O_2	0.2458 (5)	−0.0139 (2)	0.5355 (5)	3.7 (2)
O_3	0.3532 (6)	−0.1193 (2)	0.5316 (5)	4.1 (2)
O_4	0.2781 (5)	−0.0225 (2)	1.0416 (5)	3.8 (2)
O_5	0.3875 (6)	0.0687 (2)	0.8669 (6)	4.4 (2)
O_6	0.1109 (5)	0.0986 (2)	0.7089 (5)	3.5 (2)
N	0.3260 (6)	−0.1518 (2)	0.8075 (6)	3.2 (2)
C_1	0.2374 (8)	−0.0987 (3)	0.7261 (7)	2.6 (2)
C_2	0.0943 (7)	−0.0626 (3)	0.7525 (7)	2.5 (2)
C_3	0.0144 (8)	−0.1159 (3)	0.8196 (7)	2.7 (2)
C_4	−0.1564 (9)	−0.1116 (3)	0.7992 (8)	3.5 (3)
C_5	−0.218 (1)	−0.1606 (4)	0.876 (1)	4.2 (3)
C_6	−0.113 (1)	−0.2123 (4)	0.974 (1)	4.6 (4)
C_7	0.055 (1)	−0.2184 (3)	0.9937 (9)	4.0 (3)
C_8	0.1135 (8)	−0.1703 (3)	0.9145 (7)	3.1 (3)
C_9	0.2798 (8)	−0.0722 (3)	0.5879 (7)	2.9 (2)
C_{10}	0.384 (1)	−0.0978 (4)	0.386 (1)	5.3 (4)
C_{11}	0.1589 (8)	−0.0006 (3)	0.8797 (7)	2.9 (2)
C_{12}	0.235 (1)	0.0582 (3)	0.8210 (8)	3.4 (3)
C_{13}	0.167 (1)	0.1596 (3)	0.6467 (9)	5.0 (3)

TABLE II. Positional Parameters and Equivalent Isotropic Thermal Parameters of **6c** with Their Estimated Standard Deviations in Parentheses

Atom	x	y	z	B_{eq}
O_1	0.8216 (2)	0.1003 (3)	0.4252 (1)	3.50 (9)
O_2	0.9494 (2)	0.4073 (3)	0.2293 (1)	5.0 (1)
O_3	0.6003 (3)	−0.0162 (4)	0.2738 (1)	6.4 (1)
O_4	0.5666 (2)	−0.0475 (3)	0.3931 (1)	4.9 (1)
N	0.8523 (2)	0.1875 (3)	0.3021 (1)	3.4 (1)
C_1	0.8622 (3)	0.3605 (4)	0.2761 (2)	3.4 (1)
C_2	0.7522 (3)	0.4812 (4)	0.3115 (2)	3.9 (1)
C_3	0.6862 (3)	0.3600 (4)	0.3714 (1)	3.1 (1)
C_4	0.7430 (3)	0.3974 (4)	0.4488 (1)	3.0 (1)
C_5	0.7296 (3)	0.5527 (4)	0.4928 (2)	3.7 (1)
C_6	0.7950 (3)	0.5548 (5)	0.5630 (2)	3.8 (1)
C_7	0.8747 (3)	0.4000 (5)	0.5860 (2)	4.0 (1)
C_8	0.8904 (3)	0.2447 (4)	0.5425 (2)	3.6 (1)
C_9	0.8212 (3)	0.2481 (4)	0.4744 (1)	3.1 (1)
C_{10}	0.7491 (3)	0.1620 (4)	0.3584 (1)	3.0 (1)
C_{11}	0.7790 (4)	0.7215 (6)	0.6120 (2)	5.7 (2)
C_{12}	0.6331 (3)	0.0209 (4)	0.3360 (2)	3.5 (1)
C_{13}	0.4458 (4)	−0.1737 (6)	0.3781 (2)	5.6 (2)

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References and Notes

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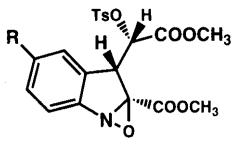
7) In the previous communication,[5] compounds **4** were assigned as oxaziridinoindoles (**7**) and **6** as furo[2,3-*b*]indoles (**8**) on the basis of spectroscopic analysis. In this paper, we wish to revise these structures on the basis of X-ray analysis.



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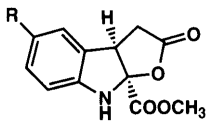

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Chart 2

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