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Studies on the Syntheses of Heterocyclic Compounds. DCCCXCII.[1] An Efficient Stereoselective Synthesis of Potential Intermediates for Rauwolfia Alkaloids from Furan and Its Derivatives

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A general method for the stereoselective synthesis of the potential intermediates (**11**), (**12**), (**20**), and (**21**) for the *Rauwolfia* alkaloid reserpine (**1**) and its analogs starting from furan and benzyl furfuryl ether is described.

Keywords——synthetic approach to reserpine; Arndt-Eistert reaction; Diels-Alder reaction of furans; halolactonization; synthesis of 3,8-epoxy-4-halo-7-oxo-2-alkoxycarbonylmethyl-6-oxabicyclo[3.2.1]octanes

Reserpine, one of the indole alkaloids of *Rauwolfia serpentina*, was first isolated in 1952.[3] The remarkable physiological properties of the alkaloid rapidly won for it an important place in the treatment of hypertensive, nervous and mental disorders. Extensive degradation and analytical studies culminated in 1955[4] in the proposal of the structure (**1**). The total synthesis of resperpine was first reported by Woodward[5] and then Pearlmann.[6]

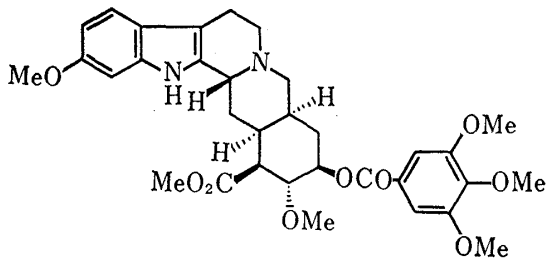

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Chart 1

In our studies towards a total synthesis of the *Rauwolfia* alkaloid reserpine (**1**) and its analogs, the lactonic ester (**2**) or its equivalent is essential for construction of the non-tryptamine moiety.

In the preceding paper,[7] we have described a general synthesis of 3,8-epoxy-4-halo-7-oxo-2-methoxycarbonylmethyl-6-oxabicyclo-[3.2.1]octane (**3**) and (**4**) starting from allene dicarboxylate and furan. Correct stereochemistry of these halolactonic esters has been proved by comparison with an authentic sample derived from the lactonic acid (**5**) and (**6**) by Arndt–Eistert reaction. Attempts to synthesize the 3-substituted lactonic ester (**2**) or its derivative resulted in the formation of the lactonic ester (**9**) because of the formation of the undesired Diels–Alder adducts (**7**) and (**8**) due to steric hindrance.

In our continuing effort to achieve the synthesis of reserpine (**1**) and its analogs, we required the preparation of the amides (**11**), (**12**), (**20**), and (**21**). Here we wish to report successful syntheses of these compounds.

As a preliminary test, we examined the synthesis of a 1-substituted 3,4-dihydro-β-carboline derivative using the known diazoketone (**10**).[7] Thus, a condensation of the diazoketone (**10**) with tryptamine or 6-methoxytryptamine in the presence of freshly prepared silver oxide afforded the corresponding amide (**11**) or (**12**), in 83.2 or 40.8% yield, respectively. When the amide (**11**) was treated with boiling phosphoryl chloride, it was smoothly converted to the 3,4-dihydro-β-carboline hydrochloride. Without purification, this salt was catalytically reduced to afford a separable mixture of compounds (**13a**) and (**13b**) whose acetylation products (**14a**) and (**14b**) were prepared and subsequently characterized. These two compounds (**13a**) and (**13b**) were produced with an approximately 1 : 1 ratio in 65% yield. Although it is obvious

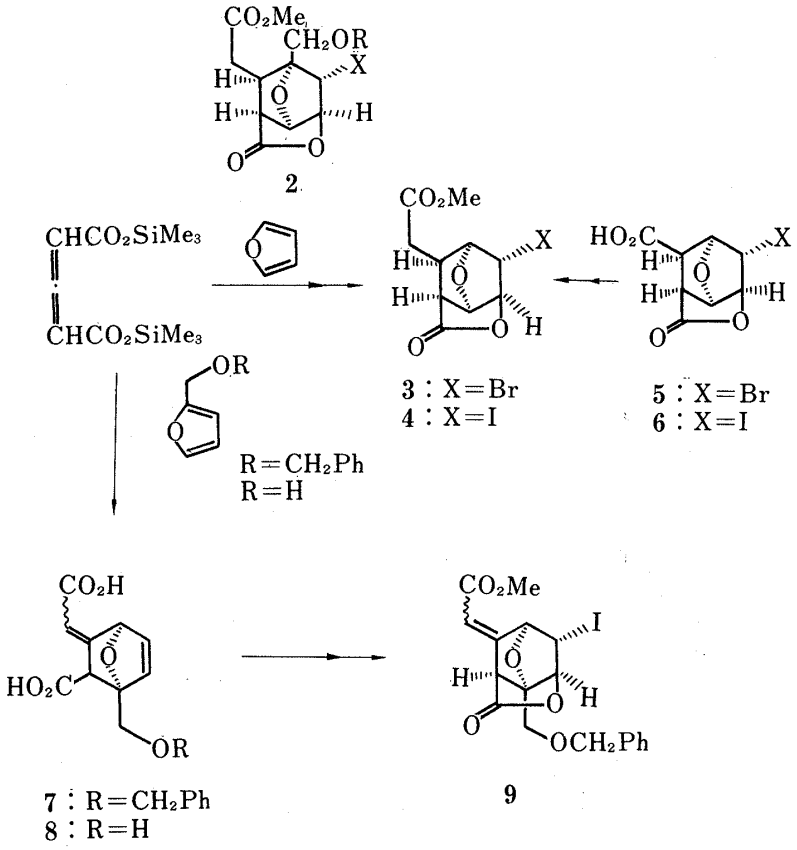


Chart 2

that these compounds are diastereoisomers at the C_1 position, it is not possible to assign configurations to (**13a**) and (**13b**) at this stage.

Although we have succeeded in the preparation of the potential intermediates, the synthesis of *Rauwolfia* alkaloids by this route is somewhat circuitous in that it is still necessary to introduce one more carbon (at C_3) at a later stage. An obviously more efficient approach to *Rauwolfia* alkaloids would be through the Diels–Alder adducts (**15**) derived from maleic anhydride and benzyl furfuryl ether.

Although a problem in this approach is the direction of halolactonization of the Diels–Alder adduct (**15**), this reaction should proceed in a desired manner because of the steric hindrance of benzyl ether at the C_3 position of the adduct (**15**).

Diels–Alder reaction of maleic anhydride with benzyl furfuryl ether in water in the presence of a catalytic amount of hydroquinone at room temperature for 7 days, followed by halolactonization without isolation of the resulting adduct, according to the method of Berson,[8] afforded the desired bromolactonic acid (**16**) and its isomer (**19**) in 18.6% overall yield based on the

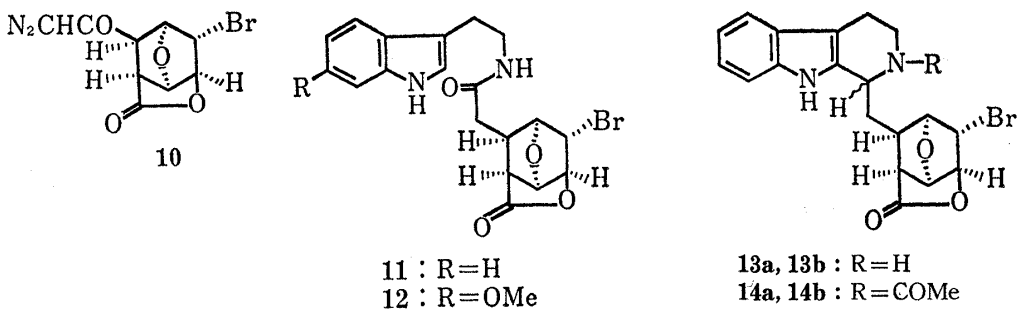
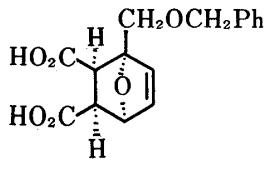


Chart 3

starting benzyl furfuryl ether. The formation ratio of (**16**) and (**19**) was approximately 2: 1. Although the yield of this Diels–Alder reaction was poor, this process is still useful because of the easy recovery of unreacted benzyl furfuryl ether from the reaction mixture. Further transformation of this acid (**16**) to the amides (**20** and **21**) by the Arndt–Eistert reaction[9] was carried out in the usual manner. Treatment of the lactonic acid (**16**) with oxalyl chloride in refluxing dry benzene gave the acid chloride (**17**) which, on reaction with diazomethane, afforded the diazoketone (**18**) in 66.5% yield. The infrared (IR) spectrum of this compound (**18**) showed a band due to the diazo group at 2140 cm^{-1} and a carbonyl band of γ-butyrolactone at 1795 cm^{-1}. Refluxing of this compound (**18**) with tryptamine or 6-methoxytryptamine in dioxane in the presence of freshly prepared silver oxide afforded the amide (**20**) or (**21**) in 98 or 65% yield, respectively. The IR spectrum of the compound (**20**) showed a band due to indole NH at 3470 and carbonyl bands of γ-butyrolactone at 1795 and amide at 1670 cm^{-1}, whereas that of compound (**21**) showed a band due to indole NH at 3450 and carbonyl bands of γ-butyrolactone at 1790 and amide at 1660 cm^{-1}. Turning to cyclization of these derivatives, it was observed that cyclization under various conditions resulted in the formation of an unnatural type of compound. Thus, Bischler–Napieralski cyclization of the amide (**20**) followed by sodium borohydride reduction of the product afforded the lactam (**22**) in 94% overall yield after purification. Formation of the lactam (**22**) can be attributed to a preference of the intermediate for the conformation (**25**) over the desired one (**24**), presumably as a result of steric hindrance of the benzyl ether group.



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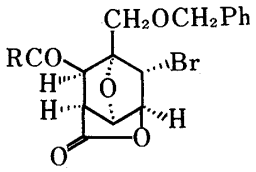
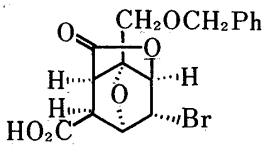


16 : R=OH
17 : R=Cl
18 : R=CHN_2



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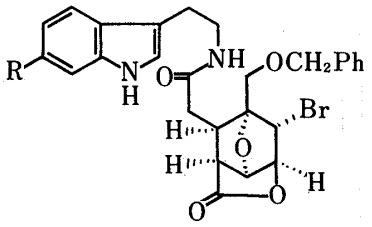
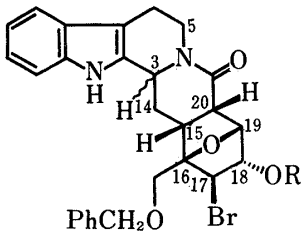
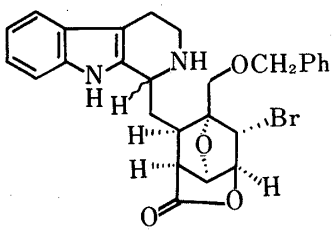


20 : R=H
21 : R=OMe



22 : R=H
23 : R=CO Me



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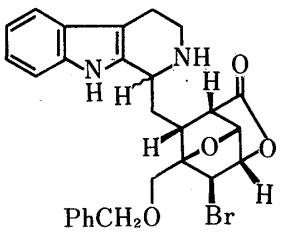

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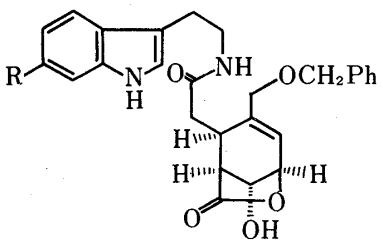

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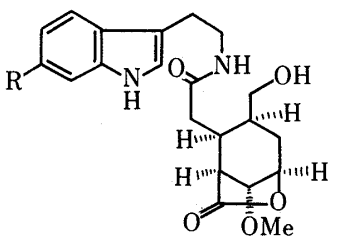

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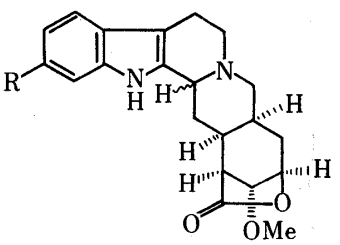

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Chart 4

Although we achieved the stereoselective syntheses of potential intermediates (**11**), (**12**), (**20**), and (**21**) which might lead to efficient stereoselective syntheses of *Rauwolfia* alkaloids, there are still some problems to be solved. One is the development of a new method for introduction of the one carbon unit at the C_3'-position in **13**. This might be achieved by alkylation of the amine nitrogen with benzenesulfonylmethyl chloride, followed by the formation of the anion which would be attacked at C_3' with simultaneous opening of the ether bond.

On the other hand, in the compounds (**20**) and (**21**), inversion of bromide, followed by reductive cleavage of the resulting bromoether would provide the compound (**26**). Catalytic hydrogenation from the less hindered side, hydrogenolysis and then methylation would give an alcohol (**27**). After formation of the D ring, Bischler–Napieralski reaction followed by sodium borohydride reduction might afford a key intermediate (**28**) leading to reserpine (**1**) and its analogs.

Thus, we achieved stereoselective syntheses of potential intermediates (**11**), (**12**), (**20**), and (**21**) which should lead to efficient stereoselective syntheses of *Rauwolfia* alkaloids.

Experimental[10]

Arndt-Eistert Reaction of 2-Diazoaceto-4-bromo-3,8-epoxy-7-oxo-6-oxabicyclo[3.2.1]octane (10) with Tryptamine——A mixture of diazoketone (**10**) (200 mg), tryptamine (118 mg) and freshly prepared silver oxide (80 mg) in dioxane (5 ml) was refluxed with stirring for 3 hr under nitrogen and then filtered to remove silver oxide. The filtrate was evaporated to leave a brown syrup, which was subjected to chromatography on silica gel. Elution with chloroform gave a crystalline solid (243 mg, 83.2%), which on recrystallization from chloroform afforded the desired amide (**11**), mp 220—222°. *Anal.* Calcd for $C_{19}H_{19}BrN_2O_4$: C, 54.29; H, 4.52; N, 6.67. Found: C, 54.40; H, 4.55, N, 6.65. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1780, 1665. NMR ($CDCl_3$) δ: 5.13 (1H, d, $J=5$ Hz, C_5–H), 5.47 (1H, t, $J=5$ Hz, C_7–H). MS *m/e*: 418, 420 (M^+).

Arndt-Eistert Reaction of 2-Diazoaceto-4-bromo-3,8-epoxy-7-oxo-6-oxabicyclo[3.2.1]octane (10) with 6-Methoxytryptamine——A mixture of diazoketone (**10**) (100 mg), 6-methoxytryptamine (70 mg) and freshly prepared silver oxide (40 mg) in dioxane (3 ml) was refluxed with stiring for 3 hr under nitrogen and the mixture was filtered to remove silver oxide. The filtrate was concentrated to leave a brown syrup, which was subjected to chromatography on silica gel. Elution with chloroform–methanol (99: 1 v/v) afforded the desired amide (**12**) (64 mg, 40.8%), mp 233—235°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1780, 1655. NMR ($CDCl_3$) δ: 3.80 (3H, s, OCH_3), 4.87 (1H, d, $J=5$ Hz, C_5–H). MS *m/e*: Calcd for $C_{20}H_{21}BrN_2O_5$: 448.0634, 450.0614. Found: 448.0671, 450.0612 (M^+).

1-(3′,8′-Epoxy-4′-bromo-7′-oxo-2′-methyl-6′-oxabicyclo[3.2.1]octane)-3,4-dihydro-β-carboline (13a and 13b)——A mixture of the amide (**11**) (100 mg) and freshly distilled phosphoryl chloride (0.4 ml) was gently refluxed with stirring for 2 hr under nitrogen. Excess phosphoryl chloride was evaporated off to leave a salt as a brown syrup, which was used in the following reaction without further purification. A solution of the salt in absolute methanol (2 ml) was hydrogenated on platinum oxide (50 mg). The mixture was filtered and the filtrate was concentrated, basified with 5% ammonium hydroxide solution, and then extracted with chloroform. The extract was washed with brine, dried over $MgSO_4$ and then evaporated to leave a yellowish brown syrup which was subjected to chromatography on silica gel (chloroform: methanol 95: 5 v/v), followed by preparative thick layer chromatography on silica gel (chloroform: methanol 9: 1 v/v) to give two 3,4-dihydro-β-carboline derivatives (**13a** and **13b**). Compound (**13a**) (32 mg), mp 199—201°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1780. NMR ($CDCl_3+CD_3OD$) δ: 4.05 (1H, s, C_4′–H), 4.59 (1H, br s, C_3′–H), 4.83 (1H, d, $J=5$ Hz, C_5′–H), 5.25 (1H, t, $J=5$ Hz, C_6′–H). MS *m/e*: 402, 404 (M^+). Compound (**13b**) (30 mg), mp 199—201°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1780. NMR ($CDCl_3+CD_3OD$) δ: 3.99 (1H, s, C_4′–H), 4.54 (1H, br s, C_3′–H), 4.81 (1H, d, $J=5$ Hz, C_5′–H), 5.25 (1H, t, $J=5$ Hz, C_6–H). MS *m/e*: 402, 404 (M^+).

Acetylation of 13a——A mixture of compound (**13a**) (2 mg), pyridine (0.1 ml) and acetic anhydride (0.1 ml) was stirred for 3 hr at room temperature. After a usual work-up, the crude product was purified by preparative thick layer chromatography (ethyl acetate: *n*-hexane 3:2 v /v) to afford a pale yellow syrup (**14a**) (1.5 mg), MS *m/e*: Calcd for $C_{21}H_{21}BrN_2O_4$: 444.0685, 446.0665. Found: 444.0681, 446.0722 (M^+).

Acetylation of 13b——A mixture of compound (**13b**) (2 mg), pyridine (0.1 ml) and acetic anhydride (0.1 ml) was treated under the same conditions as above. After a usual work-up, the crude product was purified by preparative thick layer chromatography (ethyl acetate: *n*-hexane 3: 2 v/v) to afford a pale yellow syrup (**14b**) (1.6 mg). MS *m/e*: Calcd for $C_{21}H_{21}N_2O_4Br$: 444.0685, 446.0665. Found: 444.0711, 446.0680 (M^+).

3-Benzyloxymethyl-4-bromo-3,8-epoxy-7-oxo-6-oxabicyclo[3.2.1]octane-2-carboxylic Acid (16)——A mixture of maleic anhydride (15 g), benzyl furfuryl ether (17.15 g) and hydroquinone (200 mg) in water (40 ml)

was stirred for 7 days at room temperature. Sodium hydrogen carbonate (25.7 g) was added in small portions over 15 min to the above mixture at 0° and then bromine (20 g) was added. The mixture was stirred for 2 hr at room temperature and then acidified with 20% sulfuric acid solution. A trace of sodium thiosulfate was added and the mixture was extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$ and then evaporated to leave a brown syrup which was subjected to chromatography on silica gel. Elution with chloroform afforded a mixture of (**16**) and (**19**). These two compounds could be easily separated by recrystallization from chloroform. The first colorless crystallized compound was the desired bromolactonic acid (**16**, 1.1 g) in 12.4% yield based on the consumed benzyl furfuryl ether, mp 199—200°. *Anal.* Calcd for $C_{16}H_{15}BrO_6 \cdot 0.5H_2O$: C, 49.00; H, 4.11. Found: C, 48.78; H, 3.59. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1785, 1725. NMR ($CDCl_3+CD_3OD$) δ: 3.91 (2H, s, $C\underline{H}_2OCH_2Ph$), 4.56 (2H, s, $OC\underline{H}_2Ph$), 4.87 (1H, s, C_4–H), 5.05 (1H, d, J= 5 Hz, C_5–H), 5.35 (1H, t, J=5 Hz, C_8–H), 7.24 (5H, s, ArH). MS *m/e*: 382, 384 (M^+). The second compound was its isomer (**19**) (630 mg), mp 178—180°. *Anal.* Calcd for $C_{16}H_{15}BrO_6$: C, 50.00; H, 3.90. Found: C, 50.25; H, 3.91. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1785, 1705. NMR ($CDCl_3+CD_3OD$) δ: 3.90 (2H, s, $C\underline{H}_2OCH_2Ph$), 4.60 (2H, s, $OC\underline{H}_2Ph$), 4.77 (1H, d, J=5 Hz, C_3–H), 4.65 and 4.82 (each 1H, s, C_4–H and C_5–H), 7.21 (5H, s, ArH), MS *m/e*: 382, 384 (M^+).

2-Diazoaceto-3-benzyloxymethyl-4-bromo-3,8-epoxy-7-oxo-6-oxabicyclo[3.2.1]octane (**18**)——Oxalyl chloride (1.8 ml) was added dropwise to a suspension of bromolactonic acid (**16**) (340 mg) in dry benzene (3 ml) at 0°, and the mixture was then refluxed for 4 hr under nitrogen. The solvent and excess oxalyl chloride were evaporated off *in vacuo* to leave the acid chloride (**17**), which was treated with excess diazomethane in ether for 17 hr. The solvent was evaporated off to leave a solid, which was filtered off and washed with ether to afford the practically pure diazoketone (**18**) (240 mg, 66.5%) as a pale yellow crystalline solid, mp 147—149°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1795, 2140. This diazoketone was used in the following reaction without further purification.

Arndt-Eistert Reaction of the Diazoketone (**18**) **with Tryptamine**——A mixture of the diazoketone (**18**) (20 mg), tryptamine (7.8 mg) and freshly prepared silver oxide (8 mg) in dioxane (1 ml) was refluxed with stirring for 3 hr under nitrogen. The mixture was filtered through a celite pad and the solid was washed with ether. The combined filtrate and washing was evaporated to leave a pale brown syrup which was purified by preparative thick layer chromatography (chloroform: methanol 9: 1 v/v) to afford the crystalline solid (26 mg, 98%). Recrystallization from chloroform gave the desired amide (**20**), mp 167—168°. *Anal.* Calcd for $C_{27}H_{27}BrN_2O_5$: C, 60.12; H, 5.04; N, 5.19. Found: C, 59.82; H, 4.68; N, 5.39. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3470, 1795, 1670 cm^{-1}. NMR ($CDCl_3$) δ: 3.80 (2H, s, $C\underline{H}_2OCH_2Ph$), 4.0 (1H, s, C_4–H), 4.50 (2H, s, $OC\underline{H}_2Ph$), 4.93 (1H, d, J=5 Hz, C_5–H), 5.19 (1H, t, J=5 Hz, C_6–H), 5.45—5.80 (1H, br s, NH), 6.83—7.67 (5H, m, ArH), 7.24 (5H, s, ArH), 8.84—8.24 (1H, br s, NH). MS *m/e*: 538, 540 (M^+).

Arndt-Eistert Reaction of Diazoketone (**18**) **with 6-Methoxytryptamine**——A mixture of the diazoketone (**18**) (150 mg), 6-methoxytryptamine (70 mg), and freshly prepared silver oxide (60 mg), and dioxane (4 ml) was refluxed with stirring for 3 hr under nitrogen. The mixture was filtered through a celite pad and the solid washed with ether. The combined filtrate and washing was evaporated to leave a brown syrup which was subjected to chromatography on silica gel. Elution with chloroform afforded the crystalline solid (136.3 mg, 65%) whose recrystallization from chloroform and ether gave the desired amide (**21**), mp 107—110°. *Anal.* Calcd for $C_{28}H_{29}BrN_2O_6$: C, 58.95; H, 5.09; N, 4.91. Found: C, 59.23; H, 5.27; N, 4.67. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1790, 1660. NMR ($CDCl_3$) δ: 3.73 (3H, s, OCH_3), 3.77 (2H, s, $C\underline{H}_2OCH_2Ph$), 3.97 (1H, s, C_4–H), 4.47 (2H, s, $OC\underline{H}_2Ph$), 4.87 (1H, d, J=5 Hz, C_5–H), 5.17 (1H, t, J=5 Hz, C_6–H), 5.53—5.86 (1H, br s, NH), 6.48—7.60 (4H, m, ArH), 7.23 (5H, s, ArH), 7.87—8.25 (1H, br s, NH). MS *m/e*: 568, 570 (M^+).

Preparation of the Hexacyclic Lactam (**22**)——The amide (**20**) (200 mg) was refluxed gently for 2 hr with freshly distilled phosphoryl chloride (1 ml). Excess phosphoryl chloride was removed *in vacuo* to leave a residue which was washed with ether to give the 3,4-dihydro-β-carboline hydrochloride (224 mg) as a bright-yellow solid, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630, 1790. This hydrochloride was used in the following reaction without further purification.

The above hydrochloride (40 mg) was dissolved in absolute methanol (2 ml) and treated with sodium borohydride (8.8 mg) in small portions. After 5 min, one drop of acetic acid and a small amount of water were added to the mixture. The mixture was extracted with chloroform. The extract was washed with brine, dried over $MgSO_4$ and then evaporated to leave a residue which was purified by preparative thick layer chromatography (chloroform: methanol 9: 1 v/v) to give the hexacyclic lactam (**22**) (38 mg, 94%) as a pale brown syrup, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1620. MS *m/e*: 522, 524 (M^+).

Acetylation of the Hexacyclic Lactam (**22**)——A mixture of the lactam (10 mg), acetic anhydride (0.5 ml) and pyridine (0.5 ml) was stirred for 5 hr at room temperature. A small amount of water was added and then excess acetic anhydride and pyridine were removed *in vacuo* to leave a residue which was diluted with chloroform. The organic layer was washed with brine and dried over $MgSO_4$. Removal of the solvent gave a residue which was purified by preparative thick layer chromatography (chloroform: methanol 9: 1 v/v) to afford the desired acetate (**23**) (5 mg) as a solid, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1750, 1630. NMR ($CDCl_3$) δ: 2.01 (3H, s, $OCOCH_3$), 3.25 (2H, dd, J=11.6 and 5.7 Hz, C_{20}–H), 3.68 (1H, s, C_{17}–H), 3.82, 4.05 (each 1H, d, J=10 Hz, $C\underline{H}_2OCH_2Ph$), 4.52 (1H, d, J=2.0 Hz, C_{18}–H), 4.58 (2H, s, $OC\underline{H}_2Ph$), 4.97 (1H, d, J=5.7 Hz, C_5–H), 5.07 (1H, d, J=5.7 Hz, C_3–H), 5.46 (1H, dd, J=5.7 and 2.9 Hz, C_{19}–H), 7.32 (5H, s, ArH), 7.0—7.6 (4H, m, ArH),

7.73—7.92 (1H, br s, NH). MS *m/e*: Calcd for $C_{29}H_{29}BrN_2O_5$: 564.1259, 566.1239. Found: 564.1248, 566.1209 (M^+).

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References and Notes

1) Part DCCCXCI: T. Kametani, M. Tsubuki, H. Nemoto, and K. Suzuki, *J. Am. Chem. Soc.*, in press.
2) Location: *a) Hondo, Akita 010, Japan*; *b) Aobayama, Sendai 980, Japan.*
3) J.M. Müller, E. Schlittler, and H.J. Bein, *Experientia*, **8**, 338 (1952).
4) L. Dorfman, A. Furlenmeier, C.F. Huebner, R. Lucas, H.B. MacPhyllamy, M.M. Meller, E. Schlittler, R. Schwyzer, and A.F. St.André, *Helv. Chim. Acta*, **37**, 59 (1954); C.F. Huebner, H.B. MacPhillamy, E. Schlittler, and A.F. St.André, *Experientia*, **11**, 303 (1955); E. Wenkert and L.H. Liu, *ibid.*, **11**, 302 (1955); C.F. Huebner and E. Wenkert, *J. Am. Chem. Soc.*, **77**, 4180 (1955); P.A. Diassi, F.L. Weisenborn, C.M. Dylion, and O. Wintersteiner, *ibid.*, **77**, 4687 (1955); E.E. van Tamelen and P.O. Hance, *ibid.*, **77**, 4692 (1955).
5) R.B. Woodward, F.E. Bader, H. Bickel, A.J. Frey, and R.W. Kierstead, *J. Am. Chem. Soc.*, **78**, 2023 (1956).
6) B.A. Pearlman, *J. Am. Chem. Soc.*, **101**, 6404 (1979).
7) T. Suzuki, S. Kagaya, A. Tomino, K. Unno, T. Kametani, T. Takahashi, and Y. Tanaka, *Heterocycles*, **9**, 1749 (1978); T. Suzuki, S. Kagaya, A. Tomino, K. Unno, and T. Kametani, *J. Chem. Soc. Perkin I*, in press.
8) J.A. Berson and R. Swidler, *J. Am. Chem. Soc.*, **75**, 1721 (1953).
9) W.E. Backmann and W.S. Struve, *Org. Reactions*, **1**, 38 (1942); T. Suzuki, A. Tomino, S. Kagaya, K. Unno, and T. Kametani, *Heterocycles*, **13**, 203 (1979).
10) Melting points were determined on a Yazawa microapparatus. IR spectra were recorded with a Shimadzu IR-400 spectrophotometer. Mass spectra were obtained with Hitachi M-52G and JEOL-MJS-01SG-2 spectrometers. Nuclear magnetic resonance (NMR) spectra were taken in solution in carbon tetrachloride, deuteriochloroform or deteriomethanol (tetramethylsilane as internal standard) with a JEOL JNM-PMX-60 or JEOL-PS-100 instrument.