

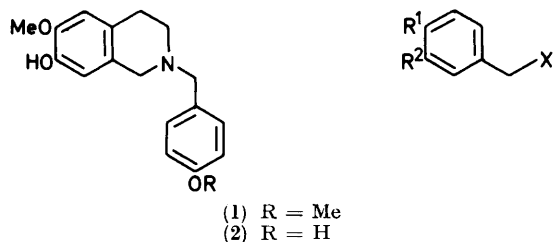
## A Novel Synthesis of the 2-Benzylisoquinoline Alkaloids, Sendaverine and Corgoine, with Aziridinium Salts as Reactive Intermediates

By **Hirota** Otomasu, **Kimio** Higashiyama, **Toshio** Honda, and **Tetsuji** Kametani,\* Hoshi College of Pharmacy, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan

A total synthesis of the 2-benzylisoquinoline alkaloids sendaverine (1) and corgoine (2) has been achieved by employing the ring-opening reaction of aziridinium salts as a key step.

AZIRIDINES and aziridinium salts are of interest, not only for theoretical reasons, but also because of their high reactivity, arising from the release of the strain energy inherent in a small ring.<sup>1</sup> It is known that aziridines and aziridinium salts are easily attacked by nucleophiles and electrophiles to give more stable ring-opened or ring-expanded products.<sup>2,3</sup>

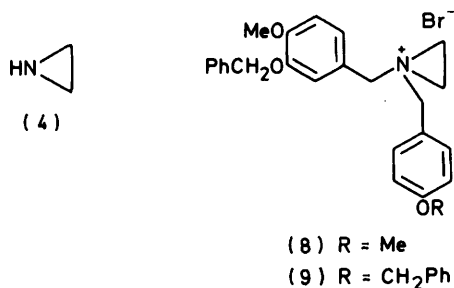
We have already reported the syntheses of the isopavine alkaloid, reframidine,<sup>4</sup> and the phthalide isoquinoline alkaloids, hydrastine and cordrastine,<sup>5</sup> both applications of this type of reaction. As an extension of this work, we have investigated the synthesis of sendaverine (1) and corgoine (2), both of which are naturally occurring 2-benzylisoquinoline alkaloids.<sup>6,7</sup>



- (3) R<sup>1</sup> = OMe, R<sup>2</sup> = OCH<sub>2</sub>Ph, X = Cl  
(5) R<sup>1</sup> = OMe, R<sup>2</sup> = OCH<sub>2</sub>Ph, X = N<sup>+</sup>  
(6) R<sup>1</sup> = OMe, R<sup>2</sup> = H, X = Br  
(7) R<sup>1</sup> = OCH<sub>2</sub>Ph, R<sup>2</sup> = H, X = Br

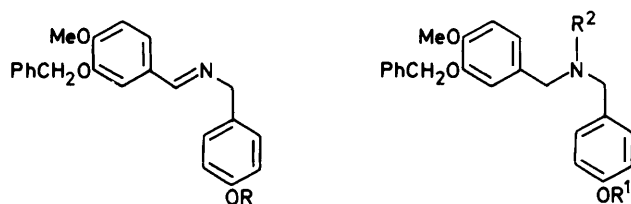
### RESULTS AND DISCUSSION

The aziridinium salts, key intermediates in the synthesis of these alkaloids, were prepared as follows. 3-Benzyloxy-4-methoxybenzyl chloride (3) was condensed with aziridine (4) in benzene in the presence of potassium carbonate to give *N*-(3-benzyloxy-4-methoxybenzyl)-aziridine (5) in 96% yield. Treatment of compound (5) with 4-methoxybenzyl bromide (6) in refluxing acetone



furnished the ring-opened bromide (10) *via* the formation of the quaternary salt (8) and subsequent nucleophilic ring-opening by the bromide ion. Similarly, the reaction of the aziridine (5) with 4-benzyloxybenzyl bromide (7) afforded the bromide (11) *via* the formation of the aziridinium salt (9), in quantitative yield. Thus, the requisite amino bromides (10) and (11) were synthesised from the chloride (3) in two steps in over 90% yield.

Since Friedel-Crafts cyclisation has been shown<sup>8</sup> to be an excellent way of constructing a tetrahydroisoquinoline nucleus, we initially investigated the intramolecular alkylation of the bromides (10) and (11) by the application of this reaction. However, the attempted conversion using aluminium chloride, boron trifluoride, or zinc chloride as cyclising reagents and methylene dichloride, nitrobenzene, carbon disulphide, or cyclohexane as solvents at appropriate temperatures, gave none of the desired product, but yielded instead the debenzylated product and decomposition products. Although the above cyclisations failed, the bromides



- (16) R = Me  
(17) R = CH<sub>2</sub>Ph  
(10) R<sup>1</sup> = Me, R<sup>2</sup> = (CH<sub>2</sub>)<sub>2</sub>Br  
(11) R<sup>1</sup> = CH<sub>2</sub>Ph, R<sup>2</sup> = (CH<sub>2</sub>)<sub>2</sub>Br  
(12) R<sup>1</sup> = Me, R<sup>2</sup> = (CH<sub>2</sub>)<sub>2</sub>OH  
(13) R<sup>1</sup> = CH<sub>2</sub>Ph, R<sup>2</sup> = (CH<sub>2</sub>)<sub>2</sub>OH  
(14) R<sup>1</sup> = Me, R<sup>2</sup> = CH<sub>2</sub>CHO  
(15) R<sup>1</sup> = CH<sub>2</sub>Ph, R<sup>2</sup> = CH<sub>2</sub>CHO  
(18) R<sup>1</sup> = Me, R<sup>2</sup> = H  
(19) R<sup>1</sup> = CH<sub>2</sub>Ph, R<sup>2</sup> = H  
(20) R<sup>1</sup> = Me, R<sup>2</sup> = CH<sub>2</sub>CH(OEt)<sub>2</sub>  
(21) R<sup>1</sup> = CH<sub>2</sub>Ph, R<sup>2</sup> = CH<sub>2</sub>CH(OEt)<sub>2</sub>

(10) and (11) were easily converted into the alcohols (12) and (13) by adsorption onto an alumina column and elution with benzene. It has been assumed that the conversion of the bromo-compounds (10) and (11) into the hydroxy-analogues (12) and (13) was facilitated by the ring-closure and ring-opening reactions of aziridines. The alcohols (12) and (13) were oxidised to the aldehydes (14) and (15) with dimethyl sulphoxide and dicyclohexylcarbodi-imide<sup>9</sup> in quantitative yields, respectively. Ring-closure of the aldehydes (14) and (15) with 10% hydrochloric acid in ethanol, and subsequent reduction

with sodium borohydride, afforded sendaverine (1) and corgoine (2), which were identical with authentic samples.<sup>10,11</sup>

Alternatively, these alkaloids were synthesised as follows. The Schiff bases (16) and (17), prepared from 3-benzyloxy-4-methoxybenzaldehyde and the corresponding benzylamines, were reduced on platinum oxide in ethanol to give the amines (18) and (19): the alkylation of these products with bromoacetaldehyde diethyl acetal in the presence of potassium carbonate afforded the acetals (20) and (21) in 31.1 and 27.7% yields, respectively. Finally, the ring-closure reaction of the ethyl acetals (20) and (21) with hydrochloric acid furnished the alkaloids (1) and (2).

Thus, the facile synthesis of sendaverine (1) and corgoine (2) has been achieved, with ring-opening reactions of the aziridinium salt as the key step; this type of reaction provides a useful route to 2-alkylisoquinolines.

#### EXPERIMENTAL

M.p.s were obtained on a Yanagimoto-Micro Melting Point apparatus and are uncorrected. I.r. spectra were measured with a 215 Hitachi Grating i.r. spectrophotometer and n.m.r. spectra with a JEOL JNM-FX 100 spectrometer using tetramethylsilane as internal reference. Mass spectra were taken with a JEOL JMS-D 300 spectrometer.

*N*-(3-Benzyloxy-4-methoxybenzyl)aziridine (5).—To a stirred solution of 3-benzyloxy-4-methoxybenzyl chloride (3) (5 g) in dry benzene (50 ml) was added aziridine (4) (30 ml) in the presence of potassium carbonate (5 g) at 0 °C. The resulting mixture was allowed to stand at room temperature while an exothermic reaction occurred. After evaporation of the solvent and the excess of reagent, the residue was diluted with water and extracted with benzene. The extract was washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated to give the residue, which was subjected to alumina (neutral) column chromatography. Elution with methylene dichloride afforded compound (5) (4.93 g, 96.2%) as colourless prisms, m.p. 62–65 °C (from hexane) (Found: C, 76.1; H, 7.2; N, 5.05. C<sub>17</sub>H<sub>19</sub>NO<sub>2</sub> requires C, 75.8; H, 7.1; N, 5.2%);  $\nu_{\max}$  (CHCl<sub>3</sub>) 1 600 and 1 595 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 1.20 (2 H, m, aziridine H), 1.76 (2 H, m, aziridine H), 3.26 (2 H, s, NCH<sub>2</sub>Ar), 3.87 (3 H, s, OMe), 5.16 (2 H, s, OCH<sub>2</sub>Ph), and 6.68–7.46 (8 H, m, ArH); *m/e* 296 (*M*<sup>+</sup>).

*N*-(3-Benzyloxy-4-methoxybenzyl)-*N*-(2-bromoethyl)-4-methoxybenzylamine (10).—A solution of the aziridine (5) (1 g) and 4-methoxybenzyl bromide (6) (0.75 g) in acetone (20 ml) was heated under reflux for 20 h. After evaporation of the solvent, the residue was chromatographed on silica gel, using methylene dichloride as eluant, to give the bromide (10) (1.65 g, 94.4%) as a colourless gum;  $\nu_{\max}$  (CHCl<sub>3</sub>) 1 605 and 1 585 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.76 (2 H, t, *J* 7 Hz, NCH<sub>2</sub>-CH<sub>2</sub>Br), 3.19 (2 H, t, *J* 7 Hz, NCH<sub>2</sub>CH<sub>2</sub>Br), 3.48 (2 H, s, NCH<sub>2</sub>Ar), 3.51 (2 H, s, NCH<sub>2</sub>Ar), 3.78 (3 H, s, OMe), 3.87 (3 H, s, OMe), 5.18 (2 H, s, OCH<sub>2</sub>Ph), and 6.77–7.45 (12 H, m, ArH); *m/e* 471 (*M*<sup>+</sup>) (Found: *M*<sup>+</sup> 471.1234. C<sub>25</sub>H<sub>28</sub>BrNO<sub>3</sub> requires *M*, 471.1233).

*N*-(3-Benzyloxy-4-methoxybenzyl)-*N*-(2-bromoethyl)-4-benzyloxybenzylamine (11).—The reaction of the aziridine (5) (1 g) with 4-benzyloxybenzyl bromide (7) (1.03 g) in acetone was carried out as above to yield the bromide (11) (1.93 g, 95.1%) as a colourless gum;  $\nu_{\max}$  (CHCl<sub>3</sub>) 1 610,

and 1 590 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.76 (2 H, t, *J* 7 Hz, NCH<sub>2</sub>CH<sub>2</sub>-Br), 3.18 (2 H, t, *J* 7 Hz, NCH<sub>2</sub>CH<sub>2</sub>Br), 3.47 (2 H, s, NCH<sub>2</sub>-Ph), 3.50 (2 H, s, NCH<sub>2</sub>Ph), 3.85 (3 H, s, OMe), 5.02 (2 H, s, OCH<sub>2</sub>Ph), 5.17 (2 H, s, OCH<sub>2</sub>Ph), and 6.79–7.43 (17 H, m, ArH); *m/e* 547 (*M*<sup>+</sup>) (Found: *M*<sup>+</sup>, 547.1536. C<sub>31</sub>H<sub>32</sub>BrNO<sub>3</sub> requires *M*, 547.1544).

*N*-(3-Benzyloxy-4-methoxybenzyl)-*N*-(2-hydroxyethyl)-4-methoxybenzylamine (12). The bromide (10) (1 g) was adsorbed onto neutral alumina (30 g). Elution with benzene afforded the alcohol (12) (0.746 g, 86.3%) as a colourless gum (Found: N, 3.3. C<sub>25</sub>H<sub>28</sub>NO<sub>4</sub> requires N, 3.4%);  $\nu_{\max}$  (CHCl<sub>3</sub>) 3 455, 1 605, and 1 585 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.01 (1 H, br s, OH), 2.54 (2 H, t, *J* 5.4 Hz, NCH<sub>2</sub>CH<sub>2</sub>OH), 3.45 (4 H, s, 2 × NCH<sub>2</sub>Ar), 3.50 (2 H, t, *J* 5.4 Hz, NCH<sub>2</sub>CH<sub>2</sub>OH), 3.77 (3 H, s, OMe), 3.86 (3 H, s, OMe), 5.15 (2 H, s, OCH<sub>2</sub>-Ph), and 6.77–7.40 (1 H, m, ArH); *m/e* 407 (*M*<sup>+</sup>) (Found: *M*<sup>+</sup> 407.2078. C<sub>25</sub>H<sub>29</sub>NO<sub>4</sub> requires 407.2095).

*N*-(3-Benzyloxy-4-methoxybenzyl)-*N*-(2-hydroxyethyl)-4-benzyloxybenzylamine (13). The bromide (11) (1 g) was chromatographed on neutral alumina (30 g) as above to furnish the alcohol (13) (0.77 g, 87.1%) as colourless leaflets, m.p. 67–69 °C (from hexane) (Found: C, 77.15 H, 6.9; N, 2.85. C<sub>31</sub>H<sub>33</sub>NO<sub>4</sub> requires C, 77.0; H, 6.85; N, 2.9%);  $\nu_{\max}$  (CHCl<sub>3</sub>) 3 455, 1 605, and 1 585 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.40 (1 H, br s, OH), 2.54 (2 H, t, *J* 5.4 Hz, NCH<sub>2</sub>CH<sub>2</sub>OH), 3.45 (4 H, s, 2 × NCH<sub>2</sub>Ar), 3.49 (2 H, t, *J* 5.4 Hz, NCH<sub>2</sub>CH<sub>2</sub>-OH), 3.87 (3 H, s, OMe), 5.03 (2 H, s, OCH<sub>2</sub>Ph), 5.16 (2 H, s, OCH<sub>2</sub>Ph), and 6.80–7.44 (17 H, m, ArH); *m/e* 483 (*M*<sup>+</sup>).

*N*-(3-Benzyloxy-4-methoxybenzyl)-*N*-(4-methoxybenzyl)-aminoacetaldehyde (14).—According to Moffatt's procedure, the alcohol (12) (0.814 g) was oxidised with dimethyl sulphoxide (6 ml) and dicyclohexylcarbodi-imide (2.48 g) in the presence of pyridinium trifluoroacetate to yield the product, which was subjected to silica gel column chromatography. Elution with methylene dichloride afforded the aldehyde (14) (0.71 g, 87.7%) as a colourless gum;  $\nu_{\max}$  (CHCl<sub>3</sub>) 1 725, 1 610, and 1 585 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 3.05 (2 H, d, *J* 2 Hz, NCH<sub>2</sub>CHO), 3.54 (4 H, s, 2 × NCH<sub>2</sub>Ph), 3.78 (3 H, s, OMe), 3.86 (3 H, s, OMe), 5.17 (2 H, s, OCH<sub>2</sub>Ph), 6.77–7.46 (12 H, m, ArH), and 9.28 (1 H, t, *J* 2 Hz, CHO); *m/e* 376 (*M*<sup>+</sup> - CHO), which is not stable enough to obtain a satisfactory microanalysis.

*N*-(3-Benzyloxy-4-methoxybenzyl)-*N*-(4-benzyloxybenzyl)-aminoacetaldehyde (15).—The oxidation of the alcohol (13) (0.966 g) was carried out as above to give the aldehyde (15) (0.79 g, 82.1%) as a colourless gum;  $\nu_{\max}$  (CHCl<sub>3</sub>) 1 725, 1 610, and 1 585 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 3.05 (2 H, d, *J* 2 Hz, NCH<sub>2</sub>CHO), 3.55 (4 H, s, 2 × NCH<sub>2</sub>Ar), 3.86 (3 H, s, OMe), 5.04 (2 H, s, OCH<sub>2</sub>Ph), 5.17 (2 H, s, OCH<sub>2</sub>Ph), 6.82–7.39 (17 H, m, ArH), and 9.29 (1 H, t, *J* 2 Hz, CHO); *m/e* 452 (*M*<sup>+</sup> - CHO).

*N*-(3-Benzyloxy-4-methoxybenzylidene)-4-methoxybenzylamine (16).—A solution of 3-benzyloxy-4-methoxybenzaldehyde (2 g) and 4-methoxybenzylamine (1.2 g) in dry benzene was heated under reflux using Dean-Stark equipment for 2 h. After evaporation of the solvent, the solid was crystallised to afford the Schiff base (16) (2.94 g, 98.6%) as colourless needles, m.p. 79–80 °C (from hexane) (Found: C, 75.45; H, 6.4; N, 3.75. C<sub>23</sub>H<sub>23</sub>NO<sub>3</sub>·0.25H<sub>2</sub>O requires C, 75.7; H, 6.45; N, 3.85%);  $\nu_{\max}$  (CHCl<sub>3</sub>) 1 640, 1 600, and 1 580 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 3.79 (3 H, s, OMe), 3.89 (3 H, s, OMe), 4.72 (2 H, s, NCH<sub>2</sub>Ar), 5.16 (2 H, s, OCH<sub>2</sub>Ph), 6.82–7.53 (12 H, s, ArH), and 8.22 (1 H, s, CH=N); *m/e* 361 (*M*<sup>+</sup>).

*N*-(3-Benzoyloxy-4-methoxybenzylidene)-4-benzoyloxybenzylamine (17).—The condensation of 3-benzoyloxy-4-methoxybenzaldehyde (2 g) and 4-benzoyloxybenzylamine (1.76 g) was carried out as above to yield the Schiff base (17) (3.56 g, 98.6%) as colourless needles, m.p. 95–96 °C (from hexane) (Found: C, 79.15; H, 6.15; N, 3.05.  $C_{29}H_{27}NO_3$  requires C, 79.6; H, 6.2; N, 3.2%);  $\nu_{\max.}$  (CDCl<sub>3</sub>) 1 640, 1 600, and 1 580 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 3.90 (3 H, s, OCH<sub>2</sub>Ph), 4.71 (2 H, s, NCH<sub>2</sub>Ph), 5.05 (2 H, s, OCH<sub>2</sub>Ph), 5.16 (2 H, s, OCH<sub>2</sub>Ph), 6.84–7.52 (17 H, m, ArH), and 8.23 (1 H, s, CH=N); *m/e* 437 (*M*<sup>+</sup>).

*N*-(3-Benzoyloxy-4-methoxybenzyl)-4-methoxybenzylamine (18).—A solution of the Schiff base (16) (1 g) in ethanol (50 ml) in the presence of platinum oxide (100 mg) was shaken at ambient temperature for 2 h under hydrogen. The catalyst was then filtered off and the filtrate concentrated to give a solid which, on recrystallisation, afforded the amine (18) (0.95 g, 94.4%) as colourless needles, m.p. 58.5–59.5 °C (from hexane) (Found: C, 76.35; H, 6.95; N, 3.8.  $C_{23}H_{25}NO_3$  requires C, 76.0; H, 6.95; N, 3.86%);  $\nu_{\max.}$  (CHCl<sub>3</sub>) 3 325, 1 605, and 1 595 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 1.45 (1 H, br s, NH), 3.67 (4 H, s, 2 × NCH<sub>2</sub>Ar), 3.77 (3 H, s, OMe), 3.86 (3 H, s, OMe), 5.14 (2 H, s, OCH<sub>2</sub>Ph), and 6.80–7.46 (12 H, m, ArH); *m/e* 363 (*M*<sup>+</sup>).

*N*-(3-Benzoyloxy-4-methoxybenzyl)-4-benzoyloxybenzylamine (19).—The reduction of the Schiff base (17) (1 g) on platinum oxide (100 mg) in ethanol (20 ml) was carried out as above to furnish the amine (19) (0.93 g, 92.6%) as colourless needles, m.p. 82–83 °C (from hexane) (Found: C, 79.4; H, 6.65; N, 3.1.  $C_{29}H_{29}NO_3$  requires C, 79.25; H, 6.65; N, 3.2%);  $\nu_{\max.}$  (CHCl<sub>3</sub>) 3 325, 1 605, and 1 580 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 1.46 (1 H, br s, NH), 3.67 (4 H, s, 2 × NCH<sub>2</sub>Ar), 3.86 (3 H, s, OMe), 5.04 (2 H, s, OCH<sub>2</sub>Ph), 5.14 (2 H, s, OCH<sub>2</sub>Ph), and 6.85–7.41 (17 H, m, ArH); *m/e* 439 (*M*<sup>+</sup>).

*N*-(3-Benzoyloxy-4-methoxybenzyl)-*N*-4-methoxybenzylaminoacetaldehyde Diethyl Acetal (20).—A mixture of the amine (18) (1 g), potassium carbonate (0.4 g), and bromoacetaldehyde diethyl acetal (5 ml) was warmed at 40 °C with stirring for 0.5 h. The resulting mixture was diluted with water and extracted with methylene dichloride. The organic layer was washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to give the residue, which was subjected to column chromatography on silica gel. Elution with methylene dichloride afforded the acetal (20) (0.41 g, 31.1%) as a colourless gum (Found: C, 73.1; H, 7.95; N, 2.85.  $C_{29}H_{37}NO_5$  requires C, 72.6; H, 7.8; N, 2.9%);  $\nu_{\max.}$  (CHCl<sub>3</sub>) 1 605 and 1 585 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 1.15 (6 H, t, *J* 7.1 Hz, 2 × OCH<sub>2</sub>CH<sub>3</sub>), 2.57 [2 H, d, *J* 5.1 Hz, NCH<sub>2</sub>CH(OEt)<sub>2</sub>], 3.44 (4 H, m, 2 × OCH<sub>2</sub>CH<sub>3</sub>), 3.53 (4 H, s, 2 × NCH<sub>2</sub>Ar), 3.77 (3 H, s, OMe), 3.86 (3 H, s, OMe), 4.50 [1 H, t, *J* 5.1 Hz, CH(OEt)<sub>2</sub>], 5.14 (2 H, s, OCH<sub>2</sub>Ph), and 6.76–7.46 (1 H, s, ArH); *m/e* 479 (*M*<sup>+</sup> – OEt).

*N*-(3-Benzoyloxy-4-methoxybenzyl)-*N*-(4-benzoyloxybenzyl)aminoacetaldehyde Diethyl Acetal (21).—The alkylation of the amine (19) (1 g) with bromoacetaldehyde diethyl acetal (5 ml) was carried out as above to yield the acetal (21) (0.35 g, 27.7%) as a colourless gum, which was crystallised as the picrate, m.p. 126–127 °C (from ethanol) (Found: C, 62.65; H, 5.7; N, 7.1.  $C_{41}H_{44}N_4O_{12}$  requires C, 62.75; H, 5.65; N, 7.15%);  $\nu_{\max.}$  (CHCl<sub>3</sub>) 1 605 and 1 585 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 1.14 (6 H, t, *J* 7.1 Hz, 2 × OCH<sub>2</sub>CH<sub>3</sub>), 2.57 [2 H, d, *J* 5.4 Hz, NCH<sub>2</sub>CH(OEt)<sub>2</sub>], 3.43 (4 H, m, 2 × OCH<sub>2</sub>CH<sub>3</sub>), 3.53 (4 H, s, 2 × NCH<sub>2</sub>Ar), 3.84 (3 H, s, OMe), 5.02 (2 H, s,

OCH<sub>2</sub>Ph), 5.14 (2 H, s, OCH<sub>2</sub>Ph), and 6.82–7.40 (17 H, m, ArH); *m/e* 510 (*M*<sup>+</sup> – OEt).

(±)-Sendaverine (1).—*Method A*. A solution of the aldehyde (14) in concentrated hydrochloric acid–ethanol (1 : 1 v/v; 20 ml) was heated under reflux for 2 h. After being cooled to room temperature, the solution was diluted with ethanol (10 ml) and the resulting mixture was basified with aqueous ammonium hydroxide. To this mixture was added sodium borohydride (0.19 g) in small portions at 0 °C and the solution was stirred at ambient temperature for 2 h. After evaporation of the solvent, the residue was diluted with water and extracted with methylene dichloride. The organic layer was washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to give a gum, which was subjected to column chromatography on silica gel. Elution with methylene dichloride afforded (±)-sendaverine (1) (0.46 g, 62.3%) as colourless needles, m.p. 139–140 °C (from hexane) (lit.,<sup>10</sup> 139–140 °C);  $\delta$ (CDCl<sub>3</sub>) 2.70 (4 H, br s, NCH<sub>2</sub>CH<sub>2</sub>), 3.45 (2 H, s, NCH<sub>2</sub>Ar), 3.57 (2 H, s, NCH<sub>2</sub>Ar), 3.72 (3 H, s, OMe), 3.78 (3 H, s, OMe), 6.47 (2 H, br s, ArH), 6.78 (2 H, d, *J* 8 Hz, ArH), and 7.22 (2 H, d, *J* 8 Hz, ArH), which was identical with an authentic specimen.

*Method B*. The cyclisation of the acetal (20) (1 g) was carried out as above to give (±)-sendaverine (1) (0.44 g, 70.5%).

(±)-Corgoine (2).—*Method A*. The cyclisation of the aldehyde (15) (1 g) with aqueous hydrochloric acid in ethanol and subsequent reduction with sodium borohydride (0.16 g) was carried out as described for the synthesis of sendaverine to yield (±)-corgoine (2) (0.28 g, 47.3%) as colourless needles, m.p. 190–191 °C (from methanol–diethyl ether) (lit.,<sup>11</sup> 190–191 °C);  $\delta$ (CF<sub>3</sub>CO<sub>2</sub>D) 3.95 (3 H, s, OMe), 6.74 (1 H, s, ArH), 6.73 (1 H, s, ArH), 7.08 (d, *J* 8 Hz, ArH), and 7.42 (2 H, d, *J* 8 Hz, ArH), which was identical with an authentic sample.

*Method B*. The cyclisation of the acetal (21) (1 g) as described above afforded (±)-corgoine (2) (0.26 g, 50.7%).

We thank Mrs. T. Ogata, Miss M. Shigetsuna, Miss M. Nagao, Mrs. A. Kumazawa, Miss H. Furuyama, and Miss Y. Narita of Hoshi College of Pharmacy for spectral measurements, microanalyses, and manuscript preparation.

[2/348 Received, 26th February, 1982]

## REFERENCES

- J. D. Cox, *Tetrahedron*, **1963**, **19**, 1175.
- D. R. Crist and N. J. Leonard, *Angew. Chem.*, **1969**, **81**, 953, and references cited therein.
- N. J. Leonard and K. Jann, *J. Am. Chem. Soc.*, **1962**, **84**, 4806.
- T. Kametani, S. Hirata, and K. Ogasawara, *J. Chem. Soc., Perkin Trans. I*, **1973**, 1466.
- T. Kametani, T. Honda, H. Inoue, and K. Fukumoto, *J. Chem. Soc., Perkin Trans. I*, **1976**, 1221.
- T. Kametani, K. Ohkubo, and S. Takano, *J. Pharm. Soc. Jpn.*, **1967**, **87**, 563.
- M. U. Ibragimova, M. S. Yunusov, and S. Yu. Yunusov, *Khim. Prirod. Soedinenii*, **1971**, **2**, 211.
- L. W. Deady, N. Pirzada, and R. D. Topsom, *J. Chem. Soc., Chem. Commun.*, **1971**, 799.
- K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **1965**, **87**, 5661, 5670.
- T. Kametani and K. Ohkubo, *Chem. Pharm. Bull. (Jpn.)*, **1967**, **15**, 608.
- T. Kametani, K. Takahashi, and C. V. Loc, *Tetrahedron*, **1975**, **31**, 235.