

## STUDIES IN THE SANDWICINE SERIES

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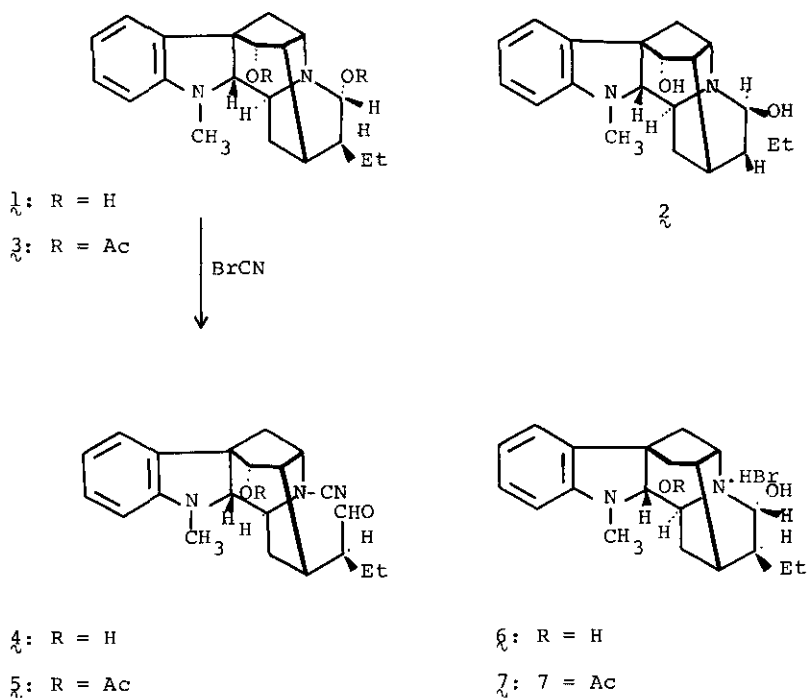
**Abstract** — As a result of studies in the correlation of structure and activity in the sandwicine series of alkaloids, a number of new derivatives have been obtained through Von Braun BrCN reaction and electrophilic substitutions in the benzene ring. The exact position of the radicals has been located through spectral studies.

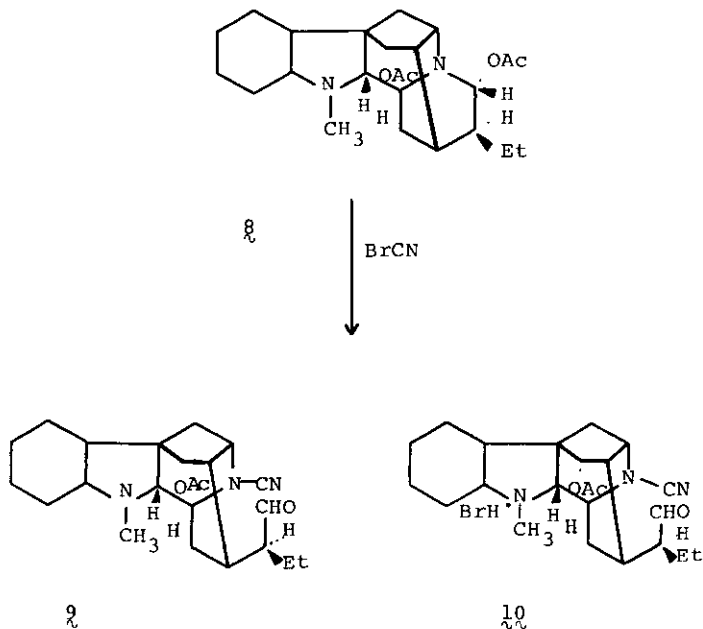
Sandwicine ( $1_{\kappa}$ ) was first isolated by Neuss et al.<sup>1</sup> in 1967 from *Rauwolfia sandwicensis*. Later it was found to occur along with isosandwicine ( $2_{\kappa}$ ) in *Rauwolfia vomitoria*.<sup>2</sup> The spectroscopic and chemical data identified sandwicine as C-17 epimer of ajmaline.<sup>1</sup> Isosandwicine, on the other hand, has different stereochemistry from ajmaline at C-17, C-20 and C-21 (17-epiisajmaline).<sup>2</sup>

In view of the increasing importance of ajmaline,<sup>3-7</sup> the main alkaloid of *Rauwolfia serpentina*, in the treatment of cardiac arrhythmias of various origins, the relationship between structure and cardiac action in the ajmaline series of bases was studied by Siddiqui et al.<sup>8,9</sup> They noted that any chemical intrusion that stabilizes either the carbinol-amine or aldehyde-imine tautomeric structure of ajmaline, greatly reduces its cardiac activity. Thus diacetyl ajmaline and methyl ajmaline show very meagre activity, indicating that carbinolamine, aldehyde-imine tautomerism serves as a cardiotropic factor. They carried out the BrCN reaction on ajmaline and its derivatives to study the comparative stability of the carbinol amine ring in them and its possible bearing on cardiac action. It was further observed that electrophilic substitutions in the benzene ring of ajmaline have a potentiating effect on the cardiac activity of ajmaline, probably by an accentuation of the dynamic character of the carbinol-amine, aldehyde-imine tautomerism of the base.<sup>8,9</sup>

In view of the likely antiarrhythmic potential of sandwicine ( $1_{\kappa}$ ) and isosandwicine ( $2_{\kappa}$ ), studies in the direction referred to above have been carried out on

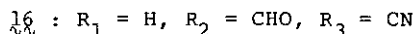
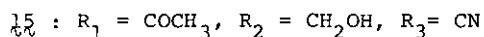
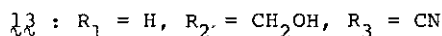
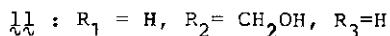
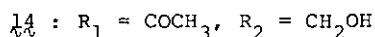
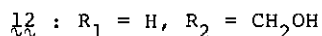
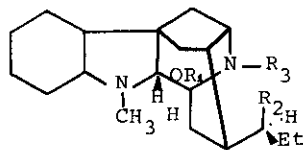
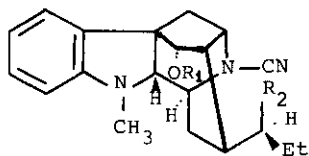
the two bases in the present work. The cyanogen bromide reaction on sandwicine and hexahydrosandwicine was undertaken, after protecting the hydroxyl groups through acetylation. Under the conditions described in the experimental, a monoacetylciano derivative (5) was readily obtained along with monoacetyl sandwicine hydrobromide (7), on the treatment of diacetyl sandwicine (3) with cyanogen bromide while the same reaction with 17,21-diacetyl hexahydrosandwicine (8) took 24 hours for completion. The comparative speed with which this reaction proceeds is a measure of the instability of the carbinol-amine ring of sandwicine and its considerable stabilization through the reduction of the benzene ring. Moreover, the reduction of benzene ring in sandwicine brings about considerable increase in the basic strength of the indole nitrogen, with the result that a stable acetylciano hexahydrosandwicine hydrobromide salt (10) was formed in the BrCN reaction with it. The cyanogen bromide reaction proceeds with the two bases on the following pattern which corresponds to the behaviour of ajmaline series of alkaloids as noted by Siddiqui and co-workers.<sup>8,9</sup>



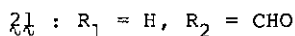
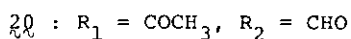
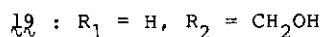
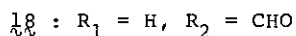
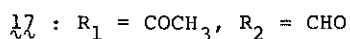
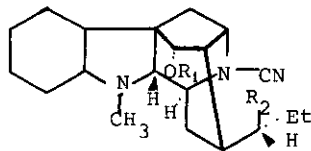
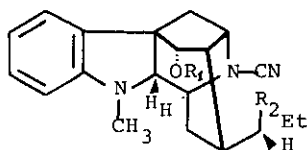


The formation of these products has been discussed at length in case of the ajmaline series of bases.<sup>8,9</sup> On mild alkaline hydrolysis of monoacetyl cyanosandwicine, the acetyl group is hydrolysed to furnish cyanosandwicine (4), while prolonged refluxing with alcoholic alkali resulted in complete hydrolysis and isomerization to isosandwicine. On the other hand when BrCN reaction was carried out with sandwicine without protecting the hydroxyl groups, the cyano derivative (4) was directly obtained along with the hydrobromide (6) of the unreacted base in 1:1 molecular proportion.

Acetyl cyano derivatives of sandwicine and hexahydrosandwicine on treatment with  $\text{LiAlH}_4$  afforded dihydrosandwicine<sup>1</sup> and unreported dihydroderivative of hexahydrosandwicine (11), respectively, by the reduction of acetate and replacement of cyano group. On the other hand borohydride reduction of aldehydic groups in acetylcyanosandwicine (5), cyanosandwicine (4), cyanohexahydrosandwicine (16) and acetylcyanohexahydrosandwicine (9) afforded the corresponding dihydro products  $\text{14}$ ,  $\text{12}$ ,  $\text{13}$  and  $\text{15}$ , respectively.



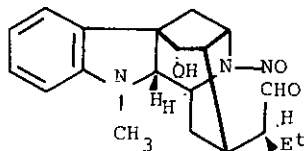
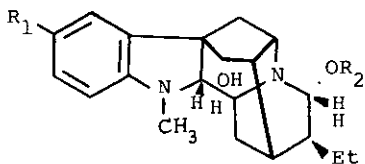
On a similar pattern of studies on isosandwicine (2), monoacetylcyano isosandwicine (17) cyanoisosandwicine (18), dihydrocyanoisosandwicine (19), monoacetylcyano hexahydroisosandwicine (20), and cyano hexahydroisosandwicine (21) were obtained.



As a result of electrophilic substitution in the benzene ring of sandwicine, bromo and sulfonic acid derivatives (22) and (23) were obtained in good yield following the procedures described in the experimental. In case of nitroso derivative it was noted that when the reaction is carried out in dilute acetic acid medium an N-nitroso derivative (26) is obtained whereas in dilute HCl a C-nitroso product (24) was formed as described in the experimental. Acetylation of sandwicine in dilute acetic acid and acetic anhydride afforded a crystalline compound in 70% yield. On the basis of spectral data it was concluded to be 21-0-acetyl sandwicine (25) although the 17-acetyl and 17,21 diacetyl sandwicine were reported<sup>1,2</sup>

to be produced by  $\text{Ac}_2\text{O}$ -pyridine treatment of **1**.

The NMR spectral studies of the substitution products indicated that groups have entered at position 10 (para to indolic N). For example the aromatic region of the NMR spectrum of **24** shows a doublet at  $\delta$  6.98 ( $J = 9.1$  c/s) and may be assigned to H-12 which has a higher electron density, shows ortho coupling with H-11 and a small para coupling with H-9 ( $J = 0.6$  c/s) visible under high resolution only. The signal of H-11 is a distorted quartet centered at  $\delta$  8.32 which is shifted downfield, due to the electron withdrawing nature of the nitroso group at C-10. It shows ortho coupling with H-12 ( $J = 9.1$  c/s) and meta coupling with H-9 ( $J = 2.5$  c/s). All other substitution products showed similar NMR pattern in the aromatic region.



**22** :  $R_1 = \text{Br}$ ,  $R_2 = \text{H}$

**23** :  $R_1 = \text{SO}_3\text{H}$ ,  $R_2 = \text{H}$

**24** :  $R_1 = \text{NO}$ ,  $R_2 = \text{H}$

**25** :  $R_1 = \text{H}$ ,  $R_2 = \text{COCH}_3$

**26**

EXPERIMENTAL

The action of cyanogen bromide on sandwicine: Sandwicine (1 g., 0.003 mole) was dissolved in dry chloroform (10 ml) and cyanogen bromide (0.43 g., 0.004 mole) in dry chloroform (4 ml) was slowly added to it with constant stirring and efficient cooling. There was no immediate precipitation but crystals began to form slowly in the cold. The reaction mixture was allowed to stand overnight, filtered and the crystalline precipitate extracted with warm 10% acetic acid. The residue left over after extraction with acetic acid crystallised out from methanolic benzene as elongated colourless needles which melted at  $243^\circ\text{C}$ , and analysed for  $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_2$  (Found: C, 71.11; H, 6.99; N, 12.1%; and  $\text{M}^+$  peak at 351.

Cyanosandwicine,  $C_{21}H_{25}N_3O_2$  required: C, 71.76; H, 7.12; N, 11.96% and mol. wt. 351).

The free base obtained from the acidic extract, failed to crystallise but could be identified as sandwicine through comparison of physical and spectral data with standard sample.

The UV spectrum of cyanosandwicine was characteristic of dihydroindoles with maxima at 246 nm (log  $\epsilon$  3.9) and 286 nm (log  $\epsilon$  3.46). The IR spectrum showed O-H stretching between 3260-3400  $cm^{-1}$ , C-H stretching of aldehydes at 2760  $cm^{-1}$ , C=N stretching at 2250  $cm^{-1}$ , C=O stretching at 1700  $cm^{-1}$  and -C-O stretching of carbinols at 1055  $cm^{-1}$ . The nmr spectrum showed peaks at  $\delta$  9.13 (1H, doublet, CHO group),  $\delta$  6.60-7.28 (4H, multiplet, aromatic protons),  $\delta$  4.12 (1H, doublet, J=9Hz, C-17 HOH),  $\delta$  3.57 (2H, multiplet, C-3H and C-5 H),  $\delta$  3.1 (1H, singlet, C-2 H) and  $\delta$  2.84 (N-CH<sub>3</sub>). The mass spectrum showed molecular ion peak at m/e 351, followed by other important fragments at m/e 336 (M-CH<sub>3</sub>)<sup>+</sup>, 333 (M-H<sub>2</sub>O)<sup>+</sup>, 323 (M-CO)<sup>+</sup>, 322 (M-CHO)<sup>+</sup> and (M-C<sub>2</sub>H<sub>5</sub>)<sup>+</sup>, in addition to peaks at m/e 200, 182, 158, 157, 145 and 144, which are common to the mass spectra of sandwicine and ajmaline.<sup>10-13</sup>

Similar work up with isosandwicine afforded cyanoisosandwicine as colourless slender needles, m.p. 228°C together with the hydrobromide of the unreacted base in almost equal proportion.

The action of cyanogen bromide on diacetyl sandwicine: Diacetyl sandwicine (lg., 0.0025 mole) was dissolved in ether with the help of a few drops of ethyl acetate, and a solution of 0.3 g. (0.0028 mole) BrCN in ether was added on to it with efficient ice cooling and stirring. The gelatinous precipitate, which separated out in the cold, was filtered and well washed with ether. The ethereal filtrate and washings were taken together and well washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and freed of the solvent. The residue crystallised from methanol in colourless prismatic rods which melted at 227-28°C and analysed for monoacetyl cyanosandwicine. (Found: C, 70.00; H, 6.92; N, 10.75% and M<sup>+</sup> peak at 393. Calculated for C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>3</sub>: C, 70.23; H, 6.87; N, 10.88% and mol.wt. 393).

The IR spectrum was identical with that of cyanosandwicine except for an additional carbonyl peak at 1730  $cm^{-1}$  and another band at 1240  $cm^{-1}$  for C-O stretching of acetate. The proton nmr spectrum showed additional peaks at  $\delta$  2.06

(3H, singlet,  $\text{OCOCH}_3$ ) and the peak for C-17  $\text{HOAC}$  appears at  $\delta$  5.71 (1H, doublet,  $J = 9\text{Hz}$ ).

The precipitate obtained in the reaction was repeatedly crystallised from methanolic acetone to give finally colourless needles which melted at  $238^\circ\text{C}$  and analysed for monoacetylsandwicine hydrobromide. (Found: C, 58.63; H, 7.00; N, 6.44; Br, 17.85%. Calcd. for  $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_3 \cdot \text{HBr}$ : C, 58.79; H, 6.68; N, 6.46; Br, 17.81%). The aqueous solution of the hydrobromide was basified with ammonia and the liberated base crystallised from methanol to afford monoacetyl sandwicine, m.p.  $153\text{--}54^\circ\text{C}$  (lit. m.p.  $153\text{--}156^\circ\text{C}$ ).<sup>1,2</sup>

Mild hydrolysis of monoacetyl cyanosandwicine: Monoacetyl cyanosandwicine (0.2 g.) was taken up in 2 c.c. methanol containing potassium hydroxide (0.02 g.) and refluxed on the water bath for half an hour. The reaction mixture was neutralised with alcoholic hydrochloric acid and the precipitated potassium chloride filtered off. On concentration of the filtrate in a rotary, colourless elongated needles, m.p.  $248^\circ\text{C}$  were obtained which could be identified with cyanosandwicine through mixed melting point.

Complete hydrolysis of monoacetyl cyanosandwicine: Monoacetylcyanosandwicine (0.5 g.) was refluxed over water bath with methanolic potassium hydroxide (5% w/v, 10 c.c.). The hydrolysis proceeded at a very slow rate with the formation of potassium acetate and evolution of ammonia. After 4 days the reaction mixture gave on keeping in the cold for 48 hours, a bulky crop of colourless crystals which was filtered, and washed with a little ice-cold methanol. It gave colourless prismatic plates which melted at  $250^\circ\text{C}$  (lit. m.p.  $250^\circ\text{C}$ )<sup>2</sup> and could be identified as isosandwicine through mixed melting point.

Hexahydrosandwicine: Sandwicine (1 g.) in 50% acetic acid was hydrogenated in the presence of Adams catalyst (0.1 g.). The absorption ceased after the uptake of 6 atoms of hydrogen per molecule of sandwicine. The catalyst was then filtered, washed with 10% acetic acid, and the combined filtrate and washings were basified with ammonia. The precipitate when filtered, washed with water and dried, crystallised out from methanol in elongated plates of hexahydrosandwicine, m.p.  $170^\circ\text{C}$ . (Found: C, 72.35; H, 9.40; N, 8.31% and  $\text{M}^+$  peak at 332. Calcd. for  $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_2$ : C, 72.29; H, 9.63; N, 8.43% and mol.wt. 332).

The IR and NMR spectra were identical with those of sandwicine with notable exception of aromatic peaks. The mass spectrum showed common features of ajmaline and

sandwicine with an increment of six units in all the fragments representing indolic moieties.

Diacetyl hexahydrosandwicine: 1 g. of hexahydrosandwicine was acetylated with acetic anhydride -pyridine to yield through usual work up diacetyl hexahydrosandwicine which crystallised from dilute alcohol, m.p. 132°C. (Found: C, 69.41; H, 8.32; N, 6.87% and  $M^+$  peak at 416. Calcd. for  $C_{24}H_{36}N_2O_4$ : C, 69.23; H, 8.65; N, 6.73% and mol.wt. 416). The IR spectrum was identical with hexahydrosandwicine except for the absence of OH bands and presence of carbonyl stretching at  $1730\text{ cm}^{-1}$ , and C-O stretching of acetate at  $1240\text{ cm}^{-1}$ . The  $^1H_1$ -nmr spectrum showed 6H singlet at  $\delta$  2.03 ( $OCOCH_3$ ), 1H doublet at  $\delta$  5.64 for C-17 HOAC and  $\delta$  5.24 (1H, broad doublet of C-21 HOAC).

Action of cyanogen bromide on diacetylhexahydrosandwicine: To an ethereal solution of diacetylhexahydrosandwicine (0.57 g., 0.0014 mole) was added drop by drop a solution of BrCN (0.2 g., 0.0019 mole) in ether (5 c.c) with efficient cooling and mechanical stirring. No immediate precipitation followed, as in the case of this reaction with diacetylsandwicine. After keeping the reaction mixture in the cold for 24 hours, a gelatinous mass settled down which was repeatedly triturated with ether. The residue left on removal of the solvent from combined ethereal extract crystallized from methanol, in colourless needles, which melted at 189°C and analyzed for monoacetylcyanohexahydrosandwicine. (Found: C, 69.71; H, 8.11; N, 10.19% and  $M^+$  peak at 399. Calcd. for  $C_{23}H_{33}N_3O_3$ : C, 69.17; H, 8.27; N, 10.52% and mol.wt. 399).

The hydrobromide salt formed in the reaction, which separated out as gelatinous mass, yielded a base which melted at 189°C and showed no depression in the melting point on admixture with the acetylcyanoderivative obtained directly from the ether soluble portion of the reaction product. The total yield of the cyano product was nearly theoretical.

Mild hydrolysis of monoacetylcyanohexahydrosandwicine - cyanohexahydrosandwicine:

The mild hydrolysis of acetyl group carried out in exactly the same manner as described for monoacetylcyanosandwicine, gave cyanohexahydrosandwicine, which crystallised out from methanol as colourless slender needles, m.p. 203°C. (Found: C, 70.81; H, 8.51; N, 11.39% and  $M^+$  peak at 357. Calcd. for  $C_{21}H_{31}N_3O_2$ : C, 70.58; H, 8.68; N, 11.76% and mol.wt. 357).



Complete hydrolysis of monoacetylcyanohexahydrosandwicine - hexahydroisosandwicine:

The complete hydrolysis of monoacetylcyanohexahydrosandwicine was achieved through methanolic alkali by following the procedure described for monoacetylcyanosandwicine. On repeated crystallisations from methanol, hexahydroisosandwicine was obtained as colourless bunches of needles which melted at 224°C and analysed for  $C_{20}H_{32}N_2O_2$ . (Found: C, 71.99; H, 9.65; N, 8.39% and  $M^+$  peak at 332. Calcd. for  $C_{20}H_{32}N_2O_2$ : C, 72.29; H, 9.63; N, 8.43% and mol.wt. 332).

The borohydride reduction of cyano derivatives:

To a solution of cyanosandwicine (0.1 g.) in ethanol (5 c.c.) was added an aqueous solution of sodium borohydride (0.2 g. in 5 c.c.) and the mixture allowed to stand overnight at room temperature. The excess of borohydride was decomposed by the addition of acetic acid (10%), and the residue left on removal of solvent was treated with cold dilute ammonia. The liberated base was extracted out with chloroform. On working up the chloroform solution cyanodihydrosandwicine was obtained on crystallization from acetone as hexagonal rods, melting at 261-62°C. (Found: C, 71.14; H, 7.71; N, 11.91% and  $M^+$  peak at 353. Calcd. for  $C_{21}H_{27}N_3O_2$ : C, 71.38; H, 7.64; N, 11.89% and mol.wt. 353). By following the above procedure, acetylcyanosandwicine, cyanoisosandwicine, cyanohexahydrosandwicine and acetyl cyanohexahydrosandwicine, were reduced to their corresponding dihydro derivatives.

Acetylcyanodihydrosandwicine: It formed colourless prismatic rods, m.p. 221-22°C and analysed for  $C_{23}H_{29}N_3O_3$  (Found: C, 69.80; H, 7.27; N, 10.82% and  $M^+$  peak at 395. Calcd. for  $C_{23}H_{29}N_3O_3$ : C, 69.87; H, 7.34; N, 10.63% and mol.wt. 395).

Cyanodihydroisosandwicine: Crystallised from methanol as colourless hexagonal plates, m.p. 237°C and analysed for  $C_{21}H_{27}N_3O_2$ . (Found: C, 71.19; H, 7.69; N, 11.82% and  $M^+$  peak at 353. Calcd. for  $C_{21}H_{27}N_3O_2$ : C, 71.28; H, 7.64; N, 11.89% and mol.wt. 353).

Dihydroderivative of cyanohexahydrosandwicine: Colourless prismatic plates from methanol. It melted at 198°C and analysed for  $C_{21}H_{33}N_3O_2$ . (Found: C, 70.28; H, 9.14; N, 11.58% and  $M^+$  peak at 359. Calcd. for  $C_{21}H_{33}N_3O_2$ : C, 70.19; H, 9.19; N, 11.70% and mol.wt. 359).

Dihydro derivative of acetyl cyanohexahydrosandwicine: It formed colourless prismatic plates from methanol, melted at 203°C and analysed for  $C_{23}H_{35}N_3O_3$  (Found: C, 68.77; H, 8.66; N, 10.81% and  $M^+$  peak at 401. Calcd. for  $C_{23}H_{35}N_3O_3$ : C, 68.82;

H, 8.72; N, 10.47% and mol.wt. 401).

The IR and  $^1\text{H}_1$ -nmr spectral data of these dihydroderivatives were identical with those of the parent bases, except for the absence of peaks due to aldehydic group and the presence of additional 2H doublet at  $\delta$  3.6 for the grouping  $-\text{CH}_2-\text{O}-\text{H}$ .

Lithium aluminium hydride reductions of acetylciano derivatives: To a solution of acetylcyanosandwicine (0.1 g.) in dry tetrahydrofuran (5 c.c.) was added an excess of lithium aluminium hydride. The reaction mixture was refluxed for 4 hours in absence of moisture ( $\text{CaCl}_2$  drying tube) and then left well corked at room temperature overnight. Excess of the hydride was destroyed by the addition of crushed ice to the cold reaction mixture which was then extracted out with ethyl acetate. The residue obtained from ethyl acetate fraction after washing, drying and removal of solvent was taken up in acetone, out of which it crystallised out on cooling as colourless long hexagonal rods, which melted at  $210-12^\circ\text{C}$  and analysed for dihydrosandwicine (Found: C, 73.21; H, 8.60; N, 8.50% and  $\text{M}^+$  peak at 328. Calcd. for  $\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}_2$ : C, 73.17; H, 8.53; N, 8.53% and mol.wt. 328). The identity was confirmed through reported melting point as well as formation of crystalline hydrobromide, m.p.  $252-53^\circ\text{C}$  (lit. m.p.  $250-255^\circ\text{C}$ ).<sup>1</sup>

Acetylcyanohexahydrosandwicine could also be reduced by the above procedure to the dihydroderivative of hexahydrosandwicine. It crystallised out from methanol as colourless rectangular plates which melted at  $174-76^\circ\text{C}$  and analysed for  $\text{C}_{20}\text{H}_{34}\text{N}_2\text{O}_2$  (Found: C, 71.72; H, 10.23; N, 8.50% and  $\text{M}^+$  peak at 334. Calcd. for  $\text{C}_{20}\text{H}_{34}\text{N}_2\text{O}_2$ : C, 71.85; H, 10.18; N, 8.38% and mol.wt. 334).

The IR and  $^1\text{H}_1$ -nmr spectral data of the dihydro derivatives were identical with those of the corresponding parent base except for additional peaks due to NH group and 2H doublet at  $\delta$  3.6 for the grouping  $-\text{CH}_2-\text{O}-\text{H}$ .

Sandwicine mono sulphonic acid: 0.4 g. sandwicine with 1 ml conc.  $\text{H}_2\text{SO}_4$  (d, 1.84; 96%) was heated at  $100^\circ\text{C}$  for 10 minutes, the reaction mixture was well cooled and diluted with cold water (7 ml), when the sulphonated product separated out in clusters of prismatic rods (0.4 g.) which did not melt upto  $360^\circ\text{C}$  and analysed for  $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_2 \cdot \text{SO}_3\text{H}$  (Found: C, 58.92; H, 6.71; N, 6.66; S, 7.97% and  $\text{M}^+$  peak at 406.  $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_2 \cdot \text{SO}_3\text{H}$  requires: C, 59.11; H, 6.40; N, 6.89; S, 7.88% and mol.wt. 406). The IR spectrum was similar to sandwicine with additional bands for S=O stretching at 1150-1165 and 1342-1350  $\text{cm}^{-1}$ . The mass spectrum showed common features of sandwicine with indolic fragments showing an increment of 80

units due to additional  $\text{SO}_3\text{H}$  group in the benzene ring. The NMR spectrum located  $\text{SO}_3\text{H}$  group at C-10.

10-bromosandwicine: A solution of sandwicine (0.75 g.) in methanol (25 ml) was acidified with a few drops of 50% acetic acid and treated with a solution of  $\text{CuBr}_2$  (0.75 g.) in methanol. The reaction mixture was stirred at room temperature for 5 hours, freed of the solvent, the residue taken up in water and basified with excess of ammonia to keep the copper salt in solution. The liberated base was shaken out with ethylacetate, which when washed, dried ( $\text{Na}_2\text{SO}_4$ ) and freed of the solvent gave a residue that crystallised from methanol, in prismatic plates, melted at  $230-2^\circ\text{C}$  and analyzed for monobromosandwicine (Found: C, 59.55; H, 6.10; N, 6.66 and Br, 19.65%. Calcd. for  $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_2\text{Br}$ : C, 59.40; H, 6.1; N, 6.93; and Br, 19.55%). The NMR spectrum revealed the position of Br at C-10 (yield 0.48 g.)

10-nitrososandwicine: Sandwicine nitrite (1 g.) was dissolved in methanol (10 ml), the solution was diluted with water (10 ml) cooled and treated with 2N hydrochloric acid (20 ml). The resulting blood red solution gradually turned brown and then green. Right at this stage, it was basified with ammonia and extracted out with ethylacetate after saturating with sodium chloride. The ethylacetate layer was washed, dried and concentrated whereby C-nitroso sandwicine was obtained as yellowish green plates which did not melt upto  $360^\circ\text{C}$  and analyzed for mononitrososandwicine. (Found: C, 67.77; H, 7.24; N, 11.67% and  $\text{M}^+$  peak at 335.  $\text{C}_{20}\text{H}_{25}\text{N}_3\text{O}_3$  required: C, 67.60; H, 7.40; N, 11.83% and mol.wt. 335). The IR spectrum was identical with sandwicine showing a strong additional band at  $1500\text{ cm}^{-1}$  for N-O stretching. Similarity with sandwicine was also shown by the mass spectrum in which all the indolic fragments showed an increment of 29 for NO group. The position C-10 could be assigned to this group on the basis of its NMR spectrum (yield 0.57 g.).

N-nitrososandwicine: A solution of sandwicine (0.5 g.) in 10% acetic acid (5 ml) was treated with an aqueous solution of sodium nitrite in the cold. The yellow crystalline precipitate which began to separate immediately was filtered, washed with dilute acetic acid and then with water, dried and recrystallized from ethylacetate. The yellowish prismatic plates of N-nitrososandwicine melted at  $210^\circ\text{C}$  and analyzed for  $\text{C}_{20}\text{H}_{25}\text{N}_3\text{O}_3$  (Found: C, 67.42; H, 7.77; N, 11.72% and  $\text{M}^+$  peak at 335.  $\text{C}_{20}\text{H}_{25}\text{N}_3\text{O}_3$  requires: C, 67.60; H, 7.40; N, 11.83% and mol.wt. 335). In the

IR spectrum it shows absorption bands at 3500 (OH), 2700 (aldehydic C-H stretching), 1700 (CO) and  $1430\text{ cm}^{-1}$  (N-NO).

21-O-acetylsandwicine: A solution of sandwicine (0.5 g.) in 10% acetic acid (3 ml) was gradually added with acetic anhydride (2 ml) with continuous vigorous stirring at room temperature. The reaction mixture was well shaken up with water till the acetic anhydride was decomposed, the solution basified with ammonia and extracted out with ethylacetate. The ethyl acetate layer was washed, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated, whereby the monoacetylated product was obtained as colourless elongated needles, which melted at  $172-4^\circ\text{C}$  and analyzed for monoacetylsandwicine (Found: C, 71.62; H, 7.85; N, 5.7%; and  $\text{M}^+$  peak at 368.  $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_3$  requires: C, 71.74; H, 7.61; N, 5.67% and mol.wt. 368). The IR spectrum showed bands at  $3400\text{ cm}^{-1}$  (OH/NH group),  $1730\text{ cm}^{-1}$  (acetyl C=O group) and  $1240\text{ cm}^{-1}$  (C-O stretching of acetates). Its Rf value differed from that of 17-O-acetyl sandwicine and was found to be 21-O-acetyl sandwicine through NMR spectral data which showed similar features as sandwicine with additional 3 protons singlet at  $\delta$  2.00 for  $\text{COCH}_3$  and a one proton doublet at  $\delta$  5.25 for 21-HOAc.

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