Studies on the Syntheses of Heterocyclic Compounds. Part 744.† A Synthesis of 1-Benzazocin-5-ones from 2,3-Dihydro-1*H*-pyrrolo[1,2-*a*]-indoles; a Synthetic Approach to the Mitomycins

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On reduction with sodium borohydride in acetic acid, the 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indoles (4) and (5) were converted into the indolines (6) and (7), which were treated with cyanogen bromide to give selectively the 5-bromo-1-cyano-1,2,3,4,5,6-hexahydro-1-benzazocines (10) and (11). The bromides (10) and (11) were transformed into 1-cyano-1,3,4,6-tetrahydro-1-benzazocin-5(2*H*)-ones (13) and (14), which underwent a transannular reaction to yield the 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indoles (4) and (5).

RECENTLY, we have reported a ready synthesis of 7-methoxymitosene [1] and desammonoapomitomycin A [2] in synthetic approaches to the mitomycins (1). The introduction of an oxy-substituent at C-9a seems to be one of the most difficult problems in this area, although photo-oxygenation of pyrrolo[1,2-*a*]indol-9-ones has afforded 9a-oxy-substituted compounds.[3] However, the transannular cyclisation of an eight-membered-ring ketone (2a) also seemed a promising approach. Lown and Itoh have reported such a reaction to give the pyrrolo[1,2-*a*]indole (5).[4] Furthermore, Kishi and his co-workers recently reported a synthesis of deiminomitomycin A by transannular cyclisation of the eight-membered ring quinone (2b).[5] We now describe the conversion of pyrrolo[1,2-*a*]indoles, easily available by known methods [1,6] and important as intermediate for the synthesis of mitosene derivatives, into 1-benzazocin-5-ones.[7]

† Part 743, T. Kametani, K. Takahashi, M. Ihara, and K. Fukumoto, *Heterocycles*, 1978, **9**, 435.

[1] T. Kametani, K. Takahashi, M. Ihara, and K. Fukumoto, *J.C.S. Perkin I*, 1976, 389.

[2] T. Kametani, K. Takahashi, Y. Kigawa, M. Ihara, and K. Fukumoto, *J.C.S. Perkin I*, 1977, 28.

[3] T. Kametani, T. Ohsawa, K. Takahashi, M. Ihara, and K. Fukumoto, *Heterocycles*, 1976, **4**, 1637; *J.C.S. Perkin I*, 1978, 460.

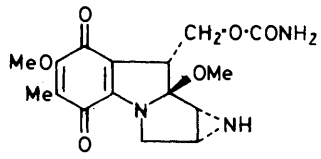
[4] J. W. Lown and T. Itoh, *Canad. J. Chem.*, 1975, **53**, 960; T. Itoh, T. Hata, and J. W. Lown, *Heterocycles*, 1976, **4**, 47.

[5] F. Nakatsubo, A. J. Cocuzza, D. E. Keeley, and Y. Kishi, *J. Amer. Chem. Soc.*, 1977, **99**, 4835.

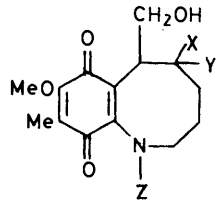
[6] G. R. Allen, jun., J. F. Polletto, and M. J. Weiss, *J. Org. Chem.*, 1965, **30**, 2897.

[7] Presented in preliminary form at the 97th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April, 1977. Abstracts of papers, II, p. 182. Preliminary communication, T. Kametani, K. Takahashi, M. Ihara, and K. Fukumoto, *Heterocycles*, 1977, **6**, 1371.

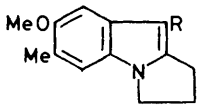
Reduction of the aldehyde (3) with sodium borohydride in glacial acetic acid [8] at 25—30 °C gave a mixture of indolines (6) and (8) as main products together with (4) and (9) as minor ones. On treatment of ketone (13) whereas the bromide (12) gave the aldehyde (15). The complicated course of reduction of the aldehyde (3) seemed to be due to the presence of the labile formyl group. Therefore the aldehyde (3) was converted



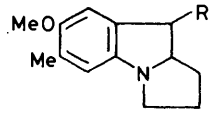
(1) mitomycin A



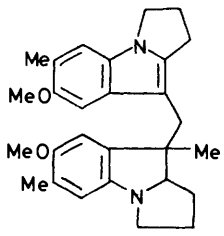
(2) a; X,Y=O, Z = CN
b; X = OMe, Y = SMe, Z = H



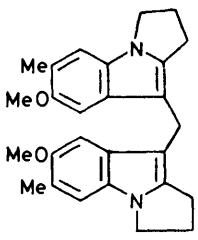
(3) R = CHO
(4) R = Me
(5) R = H



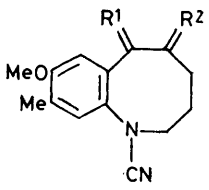
(6) R = Me
(7) R = H



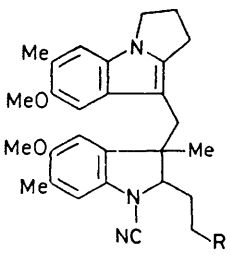
(8)



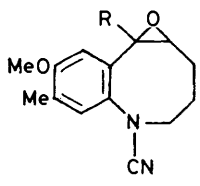
(9)



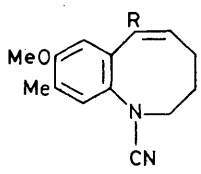
(10) R¹ = H, Me, R² = H, Br
(11) R¹ = H₂, R² = H, Br
(13) R¹ = H, Me, R² = O
(14) R¹ = H₂, R² = O
(20) R¹ = CH₂, R² = O



(12) R = CH_2Br
(15) R = CHO



(18) R = Me
(19) R = H



(16) R = Me
(17) R = H

the mixture with cyanogen bromide, compounds (6) and (8) gave the ring-opened bromides (10) and (12), respectively, the structures of which were determined by oxidation with dimethyl sulphoxide in the presence of sodium hydrogen carbonate. The bromide (10) afforded the into the methyl derivative (4) by Wolff–Kishner reduction, and the product (4) was reduced to the indoline (6) with sodium borohydride in acetic acid in high yield.

[8] G. W. Gribble, P. D. Lord, J. Skotnicki, S. E. Dietz, J. T. Eaton, and J. L. Johnson, *J. Amer. Chem. Soc.*, 1974, **96**, 7812.

Dehydrogenation of (6) with activated manganese dioxide gave back (4). Treatment of (6) with cyanogen bromide in benzene cleaved selectively the N–C(9a) bond to furnish the benzazocine derivative (10). Oxidation of (10) was carried out by heating with dimethyl sulphoxide and sodium hydrogen carbonate, but the desired ketone (13) was obtained in poor yield. The bromide (10) was therefore converted into the ketone (13) in three steps as follows. Dehydrobromination of (10) by heating with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) in tetrahydrofuran yielded the olefin (16), which was stirred with *m*-chloroperbenzoic acid in methylene chloride to give the epoxide (18). Treatment of (18) with boron trifluoride–ether in benzene at room temperature for 5 min provided the ketone (13).

The 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (5) [6] was converted into the ketone (14) in a similar manner. Reduction of (5) with sodium borohydride in acetic acid yielded quantitatively the amine (7), the von Braun reaction of which gave the bromide (11). Treatment of (11) with DBU, followed by epoxidation of the resulting (17) afforded (19), which was transformed into the ketone (14). The ketone (14) was also prepared by heating (11) with sodium hydrogen carbonate in dimethyl sulphoxide. Reaction of (14) with paraformaldehyde in the presence of sodium hydride gave the methylene derivative (20).

The ketones (13) and (14) were quantitatively converted into the pyrrolo[1,2-*a*]indoles (4) and (5) by refluxing in ethanolic sulphuric acid.

The ring opening of pyrrolo[1,2-*a*]indoles to 1-benzazocin-5-ones may well prove an important process in the synthesis of mitomycins.

EXPERIMENTAL

M.p.s were taken with a Yanagimoto micro-apparatus (MP–S2). I.r. spectra were measured with a Hitachi 215 recording spectrophotometer, n.m.r. spectra with a JEOL JNM–PMX 60 spectrophotometer, and mass spectra with a Hitachi RMU–7 spectrometer. High performance liquid chromatography (h.p.l.c.) was carried out with a Hitachi 635 instrument equipped with a 1 ft × 4 in column of μ-Bondapak C_{18}.

Reduction of 2,3-*Dihydro*-7-*methoxy*-6-*methyl*-1H-*pyrrolo*[1,2-a]*indole*-9-*carbaldehyde* (3).—To a stirred solution of the aldehyde (3) [1] (0.92 g) in acetic acid (150 ml) was added sodium borohydride (0.5 g) in small portions. After stirring for 30 min at room temperature, the mixture was diluted with water and extracted with chloroform. The organic layer was washed with water, aqueous sodium hydrogen carbonate, and aqueous sodium chloride, and dried (Na_2SO_4). Evaporation gave a syrup, which was triturated with methanol to give 2,2′,3,3′-*tetrahydro*-7,7′-*dimethoxy*-6,6′-*dimethyl*-9,9′-*methylenedi*-1H-*pyrrolo*[1,2-a]*indole* (9) as prisms, m.p. 233—234° (Found: C, 78.3; H, 7.2; N, 6.7. $C_{27}H_{30}N_2O_2$ requires C, 78.25; H, 7.3; N, 6.75%); δ($CDCl_3$) 2.26 (6 H, s, 2 × ArMe), 3.84 (6 H, s, 2 × OMe), 3.98 (2 H, s, $ArCH_2Ar$), 6.82 and 6.86 (each 2 H, each s, 4 × ArH); *m/e* 414 (M^+). The mother liquor was purified by h.p.l.c. with methanol–water (3 : 1 v/v) as solvent (flow rate 3 ml min^{-1}). The first product (6), eluted after 2 min gave a syrup, δ(CCl_4) 1.26 (3 H, d, *J* 7 Hz, 9-Me), 2.06 (3 H, s, ArMe), 3.66 (3 H, s, OMe), and 6.20 and 6.40 (each 1 H, each s, 2 × ArH); *m/e* 217 (M^+). 2,3-*Dihydro*-7-*methoxy*-6,9-*dimethyl*-1H-*pyrrole*[1,2-a]*indole* (4) was eluted after 3 min and crystallised from ether to afford prisms, m.p. 128—130° (Found: C, 77.95; H, 8.05; N, 6.45. $C_{14}H_{17}NO$ requires C, 78.1; H, 7.95; N, 6.5%); δ(CCl_4) 2.12 and 2.22 (each 3 H, each s, 2 × ArMe), 3.74 (3 H, s, OMe), and 6.60 and 6.70 (each 1 H, each s, 2 × ArH); *m/e* 215 (M^+). The third product (8), eluted after 7 min, afforded a syrup, δ(CCl_4) 1.34 (3 H, s, 9-Me), 2.04 and 2.22 (each 3 H, each s, 2 × ArMe), 3.20 and 3.68 (each 3 H, each s, 2 × OMe), and 6.08, 6.18, 6.60, and 6.78 (each 1 H, each s, 4 × ArH); *m/e* 430 (M^+) and 217 (base), which did not crystallise.

2,3-*Dihydro*-7-*methoxy*-6,9-*dimethyl*-1H-*pyrrolo*[1,2-a]-*indole* (4).—(*a*) A mixture of the aldehyde (3) (2.29 g), hydrazine hydrate (1 ml), potassium hydroxide (1.4 g), and diethylene glycol (45 ml) was refluxed for 6 h, then extracted with benzene. The extract was washed with aqueous sodium chloride, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (benzene) to give a solid, recrystallisation of which from ether afforded (4) (1.61 g, 75%) as prisms, identical (m.p., i.r., and n.m.r. spectra) with the sample described above.

(*b*) A mixture of compound (6) (200 mg), activated manganese dioxide (1.0 g), and methylene chloride (5 ml) was stirred at room temperature for 2 h in a current of nitrogen, then filtered through Celite. The Celite and inorganic material were washed with methylene chloride. The combined filtrate and washings were concentrated to leave a solid, which was recrystallised from ether to give (4) (165 mg, 83%) as prisms, identical (m.p. and spectral data) with the sample prepared by method (*a*).

5-*Bromo*-1-*cyano*-1,2,3,4,5,6-*hexahydro*-8-*methoxy*-6,9-*dimethyl*-1-*benzazocine* (10) *and* 2-(3-*Bromopropyl*)-1-*cyano*-2,3-*dihydro*-3-(2,3-*dihydro*-7-*methoxy*-6-*methyl*-1H-*pyrrolo*-[1,2-a]*indol*-9-*ylmethyl*)-5-*methoxy*-3,6-*dimethylindole* (12).—The crude product of sodium borohydride reduction of the aldehyde (3) (0.92 g) in acetic acid (150 ml) described above was dissolved in benzene (50 ml), and to the stirred solution was added cyanogen bromide (0.48 g). After stirring for 30 min in a current of nitrogen, the mixture was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel in benzene to afford a solid, recrystallisation of which from n-hexane gave (12) as *prisms* (390 mg, 36%), m.p. 199—201° (Found: C, 65.1; H, 6.45. $C_{29}H_{34}BrN_3O_2$ requires C, 64.9; H, 6.4%), $\nu_{max.}$ ($CHCl_3$) 2 210 cm^{-1} (CN); δ (CCl_4) 1.36 (3 H, s, 3-Me), 2.16 and 2.26 (each 3 H, each s, 2 × ArMe), 3.10 and 3.64 (each 3 H, each s, 2 × OMe), and 5.46, 6.14, 6.80, and 6.90 (each 1 H, each s, 4 × ArH); *m/e* 537, 535 (M^+), 323, 321, and 201 (base peak). Further elution with benzene gave a solid which was recrystallised from n-hexane to give (10) as *prisms* (330 mg, 26%), m.p. 137—138° (Found: C, 56.05; H, 5.8; N, 8.6. $C_{15}H_{19}BrN_2O$ requires C, 55.7; H, 5.9; N, 8.65%); δ (CCl_4) 1.44 (3 H, d, *J* 7 Hz, 6-Me), 2.18 (3 H, s, ArMe), 3.86 (3 H, s, OMe), and 6.76 and 7.16 (each 1 H, each s, 2 × ArH); *m/e* 324, 322 (M^+), and 201 (base peak).

5-*Bromo*-1-*cyano*-1,2,3,4,5,6-*hexahydro*-8-*methoxy*-6,9-*dimethyl*-1-*benzazocine* (10).—To a stirred solution of compound (4) (2.15 g) in acetic acid (100 ml) was added sodium borohydride (1.0 g) in small portions at room temperature. After stirring for 30 min, the mixture was diluted with water and extracted with chloroform. The extract was washed with water, aqueous sodium hydrogen carbonate, and aqueous sodium chloride, and dried (Na_2SO_4). Evaporation

afforded 2,3,9,9a-tetrahydro-7-methoxy-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole (6) as a syrup, identical (i.r. and n.m.r. spectra) with the sample described above. The product was treated with cyanogen bromide (1.2 g) in benzene (100 ml). Work-up as above gave (10) (1.4 g, 43%), identical (i.r. and n.m.r. spectra) with the sample described above.

1-*Cyano*-1,3,4,6-*tetrahydro*-8-*methoxy*-6,9-*dimethyl*-2,3-*benzazocin*-5(2H)-*one* (13).—(*a*) A mixture of the bromide (10) (320 mg), sodium hydrogen carbonate (80 mg), and dimethyl sulphoxide (10 ml) was heated at 145—150 °C for 0.5 h in a current of nitrogen. The mixture was poured into water and extracted with ether. The extract was washed with aqueous sodium chloride, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel. Elution with chloroform gave a solid which was recrystallised from ethanol to give (13) as *needles* (6 mg, 2%), m.p. 149—150° (Found: C, 68.9; H, 7.1; N, 10.6%; M^+, 258.1366. $C_{15}H_{18}N_2O_2 \cdot 0.25H_2O$ requires C, 68.5; H, 7.05; N, 10.65%. $C_{15}H_{18}N_2O_2$ requires *M*, 258.1368); δ ($CDCl_3$) 1.40 (3 H, d, *J* 7 Hz, 6-Me), 2.12 (3 H, s, ArMe), 3.80 (3 H, s, OMe), and 6.62 and 7.08 (each 1 H, each s, 2 × ArH); *m/e* 258 (M^+).

(*b*) A solution of the epoxide (18) (258 mg) and boron trifluoride–ether (0.2 ml) in benzene (10 ml) was stirred at room temperature for 5 min. The mixture was poured into water and extracted with chloroform. The extract was washed with aqueous sodium chloride, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel with benzene to give a solid, recrystallisation of which from ethanol gave (13) (105 mg, 41%) as needles, identical (i.r., n.m.r., and mass spectral data) with the above sample.

1-*Cyano*-2-(2-*formylethyl*)-2,3-*dihydro*-3-(2,3-*dihydro*-7-*methoxy*-6-*methyl*-1H-*pyrrolo*[1,2-a]*indol*-9-*ylmethyl*)-5-*methoxy*-3,6-*dimethylindoline* (15).—A mixture of the bromide (12) (214 mg), sodium hydrogen carbonate (32 mg), and dimethyl sulphoxide (10 ml) was heated at 150 °C for 15 min in a current of nitrogen, then poured into water and extracted with ether. The extract was washed with aqueous sodium chloride, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (benzene) to give a solid, which was recrystallised from n-hexane to afford (15) (110 mg, 58%) as *prisms*, m.p. 177—178° (Found: C, 73.95; H, 6.65; N, 8.7. $C_{29}H_{33}N_3O_3$ requires C, 73.85; H, 7.05; N, 8.9%); $\nu_{max.}$ ($CHCl_3$) 2 210 (CN) and 1 720 cm^{-1} (C=O); δ ($CDCl_3$) 1.36 (3 H, s, 3-Me), 2.14 and 2.22 (each 3 H, each s, 2 × ArMe), 3.08 and 3.58 (each 3 H, each s, 2 × OMe), 5.56, 6.04, 6.72, and 6.78 (each 1 H, each s, 4 × ArH), and 9.82 (1 H, s, CHO); *m/e* 471 (M^+) and 214 ($M^+ - C_{15}H_{17}N_2O_2$).

2,3,9,9a-*Tetrahydro*-7-*methoxy*-6-*methyl*-1H-*pyrrolo*[1,2-a]-*indole* (7).—To a solution of compound (5) [6] (2.6 g) in acetic acid (100 ml) was added sodium borohydride (1.3 g) in small portions during 1 h. The mixture was diluted with water and extracted with chloroform. The extract was washed with water, aqueous sodium hydrogen carbonate, and aqueous sodium chloride, dried (Na_2SO_4), and evaporated to leave a syrup, δ (CCl_4) 2.12 (3 H, s, ArMe), 3.66 (3 H, s, OMe), and 6.26 and 6.46 (each 1 H, each s, 2 × ArH); *m/e* 203 (M^+), which was used in the next step without purification.

5-*Bromo*-1-*cyano*-1,2,3,4,5,6-*hexahydro*-8-*methoxy*-9-*methyl*-1-*benzazocine* (11).—A solution of compound (7) [from 2.6 g of (5)] and cyanogen bromide (1.3 g) in benzene (300 ml) was stirred at room temperature in a current of nitrogen for 1 h. The mixture was washed with water, dried (Na_2SO_4), and evaporated to leave a solid, which was chromatographed on silica gel. Elution with benzene gave a solid, recrystallisation of which from ether afforded (11) (1.96 g, 49%) as *prisms*, m.p. 132—133° (Found: C, 54.4; H, 5.3; N, 9.25. $C_{14}H_{17}BrN_2O$ requires C, 53.9; H, 5.2; N, 9.05%); $\nu_{max.}$ ($CHCl_3$) 2 210 cm^{-1} (CN); δ (CCl_4) 2.14 (3 H, s, ArMe), 3.82 (3 H, s, OMe), and 6.66 and 7.06 (each 1 H, each s, 2 × ArH); *m/e* 310/308 (M^+).

1-*Cyano*-1,3,4,6-*tetrahydro*-8-*methoxy*-9-*methyl*-1-*benzazocin*-5(2H)-*one* (14).—(*a*) A mixture of the bromide (11) (155 mg), sodium hydrogen carbonate (80 mg), and dimethyl sulphoxide (10 ml) was heated at 145—150 °C for 1 h. Work-up as above gave the ketone (14) (8 mg, 7%) as *needles*, m.p. 127—129° (from ether) (Found: C, 68.8; H, 6.4; N, 11.4. $C_{14}H_{16}N_2O_2$ requires C, 68.85; H, 6.6; N, 11.45%); $\nu_{max.}$ ($CHCl_3$) 2 210 (CN) and 1 705 cm^{-1} (C=O); δ ($CDCl_3$) 2.16 (3 H, s, ArMe), 3.74 (2 H, s, ArCH_2), 3.80 (3 H, s, OMe), and 6.60 and 7.10 (each 1 H, each s, 2 × ArH); *m/e* 244 (M^+).

(*b*) A solution of the epoxide (19) (2.44 g) and boron trifluoride–ether (2 ml) in benzene (50 ml) was stirred at room temperature for 5 min. Work-up as above gave the ketone (14) (1.58 g, 65%) as needles, identical (m.p., i.r., and n.m.r. spectra) with the sample prepared by method (*a*).

1-*Cyano*-1,2,3,4-*tetrahydro*-8-*methoxy*-6,9-*dimethyl*-1-*benzazocine* (16).—A solution of the bromide (10) (323 mg) and 1,5-diazabicyclo[5.4.0]undec-5-ene (304 mg) in tetrahydrofuran (20 ml) was heated under reflux for 15 h in a current of nitrogen. The mixture was evaporated and the residue was chromatographed on silica gel with chloroform to give (16) (189 mg, 78%) as a syrup, $\nu_{max.}$ ($CHCl_3$) 2 220 cm^{-1} (CN); δ (CCl_4) 2.10br (3 H, s, 6-Me), 2.16 (3 H, s, ArMe), 3.80 (3 H, s, OMe), 5.50—6.00 (1 H, m, 5-H), and 6.62 and 7.02 (each 1 H, each s, 2 × ArH); *m/e* 242 (M^+), which did not crystallise.

1-*Cyano*-1,2,3,4-*tetrahydro*-8-*methoxy*-9-*methyl*-1-*benzazocine* (17).—A solution of the bromide (11) (1.5 g) and 1,5-diazabicyclo[5.4.0]undec-5-ene (1.5 g) in tetrahydrofuran (50 ml) was heated under reflux for 15 h in a current of nitrogen. Work-up as above gave (17) (1.02 g, 89%) as a syrup, $\nu_{max.}$ ($CHCl_3$) 2 220 cm^{-1} (CN); δ (CCl_4) 2.16 (3 H, s, ArMe), 3.76 (3 H, s, OMe), 5.50—6.00 (1 H, m, 5-H), 6.36 (1 H, d, *J* 10 Hz, 6-H), and 6.44 and 7.02 (each 1 H, each s, 2 × ArH); *m/e* 228 (M^+), which did not crystallise.

1-*Cyano*-5,6-*epoxy*-1,2,3,4,5,6-*hexahydro*-8-*methoxy*-6,9-*dimethyl*-1-*benzazocine* (18).—A solution of the olefinic compound (16) (242 mg) and *m*-chloroperbenzoic acid (350 mg) in methylene chloride (10 ml) was stirred at room temperature for 15 h in a current of nitrogen. The solution was washed with aqueous sodium hydrogen sulphite, aqueous sodium hydrogen carbonate, and aqueous sodium chloride. The organic layer was evaporated to give a solid, recrystallisation of which from ether gave (18) (189 mg, 73%) as *needles*, m.p. 186—188° (Found: C, 69.5, H, 7.1; N, 10.75. $C_{15}H_{18}N_2O_2$ requires C, 69.75; H, 7.0; N, 10.85%); $\nu_{max.}$ ($CHCl_3$) 2 220 cm^{-1} (CN); δ ($CDCl_3$) 1.70 (3 H, s, 6-Me), 2.20 (3 H, s, ArMe), 3.86 (3 H, s, OMe), and 6.86 and 7.04 (each 1 H, each s, 2 × ArH); *m/e* 258 (M^+).

1-*Cyano*-5,6-*epoxy*-1,2,3,4,5,6-*hexahydro*-8-*methoxy*-9-*methyl*-1-*benzazocine* (19).—A solution of the olefinic compound (17) (228 mg) and *m*-chloroperbenzoic acid (350 mg) in methylene chloride (10 ml) was stirred at room temperature for 15 h in a current of nitrogen; work-up as above gave a solid, recrystallisation of which from ether afforded (19) (204 mg, 84%) as *needles*, m.p. 153—154° (Found: C, 68.65;

H, 6.45; N, 11.55. $C_{14}H_{16}N_2O_2$ requires C, 68.85; H, 6.6; N, 11.45%); $\nu_{max.}$ ($CHCl_3$) 2 220 cm^{-1} (CN); δ ($CDCl_3$) 2.16 (3 H, s, ArMe), 3.84 (3 H, s, OMe), and 6.86 and 6.92 (each 1 H, each s, 2 × ArH); *m/e* 244 (M^+).

1-*Cyano*-1,3,4,6-*tetrahydro*-8-*methoxy*-9-*methyl*-6-*methylene*-1-*benzazocin*-5(2H)-*one* (20).—A stirred mixture of the ketone (488 mg) and 50% sodium hydride (100 mg) in tetrahydrofuran (10 ml) was treated with gaseous formaldehyde under ice cooling. The mixture was stirred at −20 °C for 30 min. An excess of ammonium chloride was added and the mixture was extracted with chloroform. The extract was chromatographed on silica gel (chloroform) to give a solid, recrystallisation of which from ethanol gave (20) (320 mg, 63%) as *needles*, m.p. 147—148° (Found: C, 68.05; H, 6.25; N, 10.45%; M^+, 256.1207. $C_{15}H_{16}N_2O_2 \cdot 0.5\ H_2O$ requires C, 67.9; H, 6.45; N, 10.55%. $C_{15}H_{16}N_2O_2$ requires *M*, 256.1211); $\nu_{max.}$ ($CHCl_3$) 2 220 cm^{-1} (CN); δ (CCl_4) 2.22 (3 H, s, ArMe), 3.86 (3 H, s, OMe), 5.66 and 6.08 (each 1 H, each d, *J* 2 Hz, 2 × olefinic H), and 6.78 and 7.16 (each 1 H, each s, 2 × ArH); *m/e* 256 (M^+).

Transannular Cyclisation of 1-*Cyano*-1,3,4,6-*tetrahydro*-8-*methoxy*-9-*methyl*-1-*benzazocin*-5(2H)-*one* (14).—A solution of the ketone (14) (49 mg) and aqueous 10% sulphuric acid (1 ml) in ethanol (5 ml) was refluxed for 2 h. The mixture was diluted with water, basified with aqueous sodium hydrogen carbonate, and extracted with chloroform. The organic layer was washed with aqueous sodium chloride solution, dried (Na_2SO_4), and evaporated to leave a solid, recrystallisation of which from methanol gave (5) (37 mg, 93%) as needles, m.p. 116—117° (lit.,[6] 116—118°), with i.r. and n.m.r. spectra identical with those of a sample prepared by a known method.

Transannular Cyclisation of 1-*Cyano*-1,3,4,6-*tetrahydro*-8-*methoxy*-6,9-*dimethyl*-1-*benzazocin*-5(2H)-*one* (13).—A solution of the ketone (13) (51 mg) and aqueous 10% sulphuric acid (1 ml) in ethanol (5 ml) was refluxed for 2 h. Work-up as above gave a solid, which was recrystallised from ether to give (4) as needles (38 mg, 88%), m.p. 128—129°, identical with the sample described above.

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