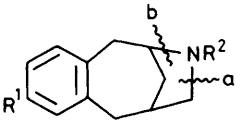
Bridged-ring Nitrogen Compounds. Part 6.[1] Synthesis of the 2,5-Methano-3-benzazocine Ring-system

Stephen J. Miller and George R. Proctor *
Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL
David I. C. Scopes
Chemical Research Department, Glaxo Group Research, Ware, Herts. SG12 0DJ

A novel synthesis of 8,8-bisethoxycarbonyl-6,7,8,9-tetrahydrobenzocyclohepten-5-one and its 2-methoxy-analogue is presented. Each was converted into the corresponding 8-carboxy-6,7,8,9-tetrahydrobenzocyclohepten-5-one which were converted into amides and thence by way of 6-bromoketo-amides to the keto-lactams: 2-benzyl-1,2,3,4,5,6-hexahydro-2,5-methano-3-benzazocine-1,4-dione and 1,2,3,4,5,6-hexahydro-8-methoxy-3-methyl-2,5-methano-3-benzazocine-1,4-dione. These, in turn, were reduced *via* lactams to 3-benzyl-1,2,3,4,5,6-hexahydro-2,5-methano-3-benzazocine and 1,2,3,4,5,6-hexahydro-8-methoxy-3-methyl-2,5-methano-3-benzazocine respectively.

Apart from one brief description,[2] derivatives of the 2,5-methano-3-benzazocine ring system (1) were unknown, although they are isomers of benzomorphans (2) and therefore of interest as potential analgesics. In this paper we describe a viable synthesis of the ring system (1); very recently an alternative synthesis has been published.[3]



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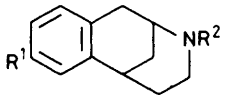

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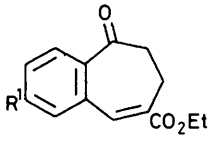

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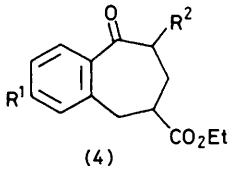

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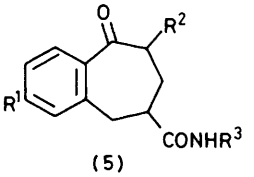

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Results and Discussion

Initially we were attracted to the synthetical strategy previously mentioned [2] (1; bond disconnection a) proceeding by oximation of compound (3; R^1 = OMe); since this proved capricious however we turned to variations involving the tetrahydrobenzocycloheptenone [2] (4; R^1 = OMe; R^2 = H). Strangely the latter compound could not be oximated although we were able to repeat published oximation work on simpler tetrahydrobenzocycloheptenones.[4] The bromo-ketones (4; R^2 = Br, R^1 = H, OMe) were easily obtained but failed to react with a variety of nitrogen nucleophiles such as azide, nitrite, and amines: we therefore conclude that the ester group at C-8 provides some unexpected steric hindrance. It was, therefore, necessary to explore an alternative strategy involving bond disconnection b (1) for which precedent exists in the benzomorphan series.[5]

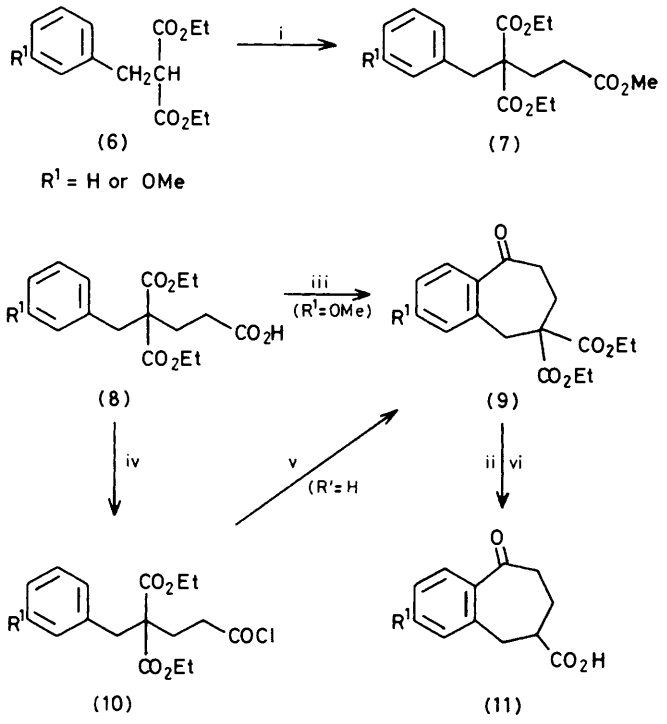
Hitherto we had obtained the ester (4; R^1 = OMe, R^2 = H) by a reduction/re-oxidation sequence from compound (3; R^1 = OMe) but this was cumbersome for larger scale working: a more efficient, versatile procedure was developed (Scheme). While this work was in progress, a similar procedure involving nitrile cyclisation was published.[6] An essential feature of our synthesis is the preferential hydrolysis of a methyl ester in presence of ethyl ester groups.[7] The benzyl malonates required as starting materials (see Scheme) were obtained either by benzylation of diethyl sodiomalonate [8] or by condensation of the aryl aldehyde with diethyl malonate followed by catalytic hydrogenation.[9]

In the case where R^1 was OMe (9; R^1 = OMe), intramolecular cyclisation was best brought about (73%) through the agency of phosphorus pentoxide in methanesulphonic acid.[7,10]

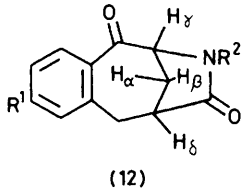
The amides (5) required for the next step of this synthesis were best obtained by coupling the corresponding acids (11; R^1 = H, OMe) with amines in presence of 2-chloro-1-methylpyridinium iodide.[11] In this way, we obtained the benzylamides (5; R^1 = R^2 = H, R^3 = $PhCH_2$) and (5; R^1 = OMe, R^2 = H, R^3 = Me) which were brominated to give in each case, a pair of diastereoisomers (5; R^1 = H, R^2 = Br, R^3 = $PhCH_2$) and (5; R^1 = OMe, R^2 = Br, R^3 = Me) which were not separated. Somewhat surprisingly, the mixtures of diastereoisomeric bromides reacted with sodium methoxide in methanol to give products (12) in greater than 90% yield: this is in contrast to experience [5] in the benzomorphan series where it was demonstrated that only the *trans*-isomer would cyclise. We attribute our success to a base-induced epimerisation fortuitously converting *cis*- into *trans*-isomers.

The structures of compounds (12; R^1 = H, R^2 = $PhCH_2$) and (12; R^1 = OMe, R^2 = Me) were amply confirmed by spectroscopic data; in particular, a characteristic upfield doublet (δ 2.0) in the ^1H n.m.r. spectra attributable to proton(s) H_α [see structure (12)] lying in the region of anisotropic shielding caused by the fused benzene ring. Models show that the uncomplicated splitting associated with H_α can be attributed to the *ca.* 90° dihedral angle between this proton and both protons H_χ and H_δ at the bridgehead.

Reduction of compound (12; R^1 = H, R^2 = CH_2Ph) by lithium aluminium hydride either alone or with aluminium chloride gave the hydroxy-amine (13) as a mixture of diastereoisomers. Reoxidation of compound (13) to the corresponding



Scheme *Reagents*: i, CH_2=$CHCO_2Me$/NaH; ii, NaOH–H_2O/THF; iii, P_2O_5/$MeSO_3H$; iv, $SOCl_2$; v, $AlCl_3$/CH_2Cl_2; vi, H_2SO_4/H_2O/heat



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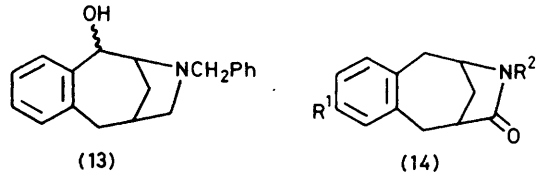
amino-ketone proved capricious: use of dimethyl sulphoxide with acetyl bromide or oxalyl chloride [12] gave what was believed to be the desired product partly purified by thick-layer silica chromatography. Likewise, chromium trioxide in pyridine [13] also oxidised compound (13) but there were several by-products and the apparent instability of the amino-ketone to air frustrated attempts to obtain material of analytical purity.

By contrast, Wolff-Kishner reduction of compounds (12; R^1 = H, R^2 = CH_2Ph) and (12; R^1 = OMe, R^2 = Me) proceeded smoothly in 65 and 61% yield respectively giving the lactams (14; R^1 = H, R^2 = CH_2Ph) and (14; R^1 = OMe, R^2 = Me). Interestingly, each of these lactams exhibited two carbonyl peaks in their i.r. spectra; a study of models reveals that this phenomenon may be attributed to the presence of two conformational isomers.

The final step in the synthesis required lithium aluminium hydride (THF) reduction of the lactams (14; R^1 = H, R^2 = CH_2Ph) and (14; R^1 = OMe, R^2 = Me) which proceeded uneventfully in excellent yield (88—90%). The products (1; R^1 = H, R^2 = $PhCH_2$) and (1; R^1 = OMe, R^2 = Me) were both distillable, slightly unstable oils which gave crystalline methiodides. All spectroscopic data (see Experimental section) were consistent with the formulations given. Thus a viable synthesis of hexahydro-2,5-methano-3-benzazocines has been discovered.



Experimental

8-Carboxy-6,7,8,9-tetrahydro-2-methoxybenzocyclohepten-5-one (11; R^1 = MeO).—The keto-ester (4; R^1 = R^2 = H) (2.10 g, 8.0 mmol) was treated with sodium hydroxide (2 g) in aqueous tetrahydrofuran (50 cm^3; 1 : 1 v/v) under reflux for 2 h. After concentration under reduced pressure and dilution with water the acid was precipitated (addition of concentrated hydrochloric acid) and then extracted (chloroform). After washing (water) and drying (Na_2SO_4) of the combined extracts, solvent was removed under reduced pressure to give an off-white *product* (1.76, 94%). Recrystallisation of this from ethyl acetate gave white needles, m.p. 152—153 °C (Found: C, 66.75; H, 6.15. $C_{13}H_{14}O_4$ requires C, 66.65; H, 6.05%), $\nu_{max.}$ (Nujol) 3 300—3 550br (OH), 1 710 (acid C=O), and 1 668 cm^{-1} (aryl C=O); δ 2.05 (2 H, m, 7-CH_2), 2.4—3.2 (5 H, m, 8-H, 6- and 9-CH_2), 3.79 (3 H, t, CH_3O), 6.4—7.2 (2 H, m, 1- and 3-H), 7.75 (1 H, d, 4-H), and 10.2 (1 H, br, s, exchangeable, OH).

8-Carbamoyl-6,7,8,9-tetrahydro-2-methoxybenzocyclohepten-5-one (5; R^1 = OMe, R^2 = R^3 = H).—The keto-acid (11; R^1 = H) (1.30 g, 5.6 mmol) was refluxed with thionyl chloride (2 cm^3) in benzene (20 cm^3) for 30 min. The solvent and excess of thionyl chloride were removed under reduced pressure (the latter by azeotroping with benzene) and the crude acid chloride was then treated (without purification), cautiously and with constant stirring, with concentrated ammonia (20 cm^3). The mixture was evaporated to dryness under reduced pressure and water and dichloromethane were added to the residue; the mixture was then washed with dilute aqueous sodium hydrogencarbonate and water. After drying (Na_2SO_4) and concentration of the extract under reduced pressure, a brown gum was obtained which crystallised from ethyl acetate as yellow platelets (0.22 g, 17%), m.p. 169—170 °C (Found: C, 66.9; H, 6.45; N, 5.95. $C_{13}H_{15}NO_3$ requires C, 66.95; H, 6.50; N, 6.0%), $\nu_{max.}$ (Nujol) 3 400, 3 180 (NH), 1 677 (aryl C=O), 1 652 (amide C=O), and 1 600 cm^{-1} (C ⋯ C); δ[$(CD_3)_2SO$] 1.85 (2 H, m, 7-CH_2), 2.4—3.2 (5 H, m, 8-H, 6-CH_2, 9-CH_2), 3.75 (3 H, s, CH_3O), 6.75 (2 H, m, 1- and 3-H), and 6.9—7.3 (2 H, 2 s, exchangeable, 2 NH), and 7.55 (1 H, d, 4-H).

Methyl 4,4-Bisethoxycarbonyl-5-phenylpentanoate (7; R^1 = H).—The diester (6; R^1 = H) (3.0 g, 12.0 mmol) was stirred overnight at room temperature with methyl acrylate (1.03 g) and sodium hydride (0.2 g; 50% dispersion in oil). After the addition of chloroform, followed by washing with 2M-hydrochloric acid and then water, the solution was dried (Na_2SO_4), and concentrated under reduced pressure to yield the product, as a colourless *oil* (3.99 g, 99%), b.p. 175 °C at 0.03 mmHg (Found: C, 64.05; H, 7.35. $C_{13}H_{24}O_6$ requires C, 64.25; H, 7.2%), $\nu_{max.}$ (film) 1 725—1 735 cm^{-1} (2 ethyl ester C=O, and methyl ester C=O); δ 1.3 (6 H, t, 2 × CH_3CH_2), 2.3 (4 H, m, 2- and 3-CH_2), 3.2 (2 H, s, 5-CH_2), 3.6 (3 H, s, CH_3O), 4.2 (4 H, q, 2 × CH_2CH_3), and 7.2 (5 H, m, aryl-H).

4,4-Bisethoxycarbonyl-5-phenylpentanoic Acid (8; R^1 = H).—The triester (7; R^1 = H) (2.0 g, 5.9 mmol) was stirred at room temperature overnight with sodium hydroxide (0.22 g)

in aqueous tetrahydrofuran (20 cm^3; 1 : 1 v/v). After the mixture had been concentrated and diluted with water (100 cm^3), the small amount of unchanged starting material was extracted by washing with toluene. Concentrated hydrochloric acid was added to the aqueous layer and the acid was extracted with dichloromethane. Following washing (water), drying (Na_2SO_4) and then concentration under reduced pressure the semisolid *product* was obtained (1.82 g, 95%). Distillation (200 °C at 0.02 mmHg) gave an analytical sample (Found: C, 63.75; H, 6.9. $C_{17}H_{22}O_6$ requires C, 63.35; H, 6.9%), $\nu_{max.}$ (film) 3 100—3 550br (OH), 1 735 (ester C=O), and 1 710 cm^{-1} (acid C=O); δ 1.15 (6 H, t, 2 × CH_3CH_2), 2.0—2.4 (4 H, m, 2,3-CH_2), 3.15 (2 H, 2,5-CH_2), 4.2 (4 H, q, 2 × CH_2CH_3), 7.2 (5 H, m, aryl), and 9.4 (1 H, s, exchangeable OH).

4,4-*Bisethoxycarbonyl*-5-*phenylpentanoyl Chloride* (10; R^1 = H).—The mono-acid (8; R = H) (2.02 g, 6.27 mmol) was refluxed with thionyl chloride (3.0 cm^3) in dry dichloromethane (10 cm^3) for 3 h after which the solvent and excess of thionyl chloride were removed under reduced pressure (azeotroping with dry toluene) to leave the crude acid chloride; this was unstable, but suitable for immediate use in the next stage of the reaction sequence; $\nu_{max.}$ 1 785 (acid chloride C=O) and 1 725 cm^{-1} (ester C=O); δ 1.2 (6 H, 2t, CH_3CH_2), 2.1 (2 H, t, 3-CH_2), 2.95 (2 H, t, 2-CH_2), 3.2 (2 H, s, 5-CH_2), 4.1 (4 H, q, 2 × CH_2CH_3), and 7.1 (5 H, m, aryl-H).

8,8-*Bisethoxycarbonyl*-6,7,8,9-*tetrahydrobenzocyclohepten*-5-*one* (9; R^1 = H).—The freshly prepared acid chloride (10; R = H) (13.0 g, 38 mmol) in dry dichloromethane (30 cm^3) was stirred with aluminium chloride (14.2 g) at −50 °C for 1.5 h. The mixture was then allowed to rise to a temperature of 0 °C and was then stirred for a further 3 h. 6M-Hydrochloric acid (50 cm^3) was added to the mixture which was then stirred for 15 min. After separation and repeated extraction of the aqueous layer with dichloromethane, the combined organic extracts were washed with 6M-hydrochloric acid and then with dilute sodium hydrogen carbonate and finally with water. After drying (Na_2SO_4), filtering (Kieselguhr) [the filter cake was soaked thoroughly in dichloromethane–ethanol and the decanted liquors filtered (paper)], and evaporation under reduced pressure of the combined liquors, a crude semisolid gum was obtained; this on distillation (160 °C at 0.02 mmHg) gave a slightly yellow solid (6.75 g, 58%). Recrystallisation [from light petroleum (b.p. 60—80 °C)] gave white needles, m.p. 64—65 °C (Found: C, 67.35; H, 6.5%; M^+, 304.1301. $C_{17}H_{20}O_5$ requires C, 67.1; H, 6.6%; M, 304.1311), $\nu_{max.}$ (Nujol) 1 720 (ester C=O), 1 675 (aryl C=O), and 1 600 cm^{-1} (C ⋯ C); δ 1.25 (6 H, t, 2 × CH_3CH_2), 2.3 (2 H, m, 7-CH_2), 2.8 (2 H, m, 6-CH_2), 3.4 (2 H, s, 9-CH_2), 4.15 (4 H, q, 2 × CH_2CH_3), and 7.3—7.65 (4 H, m, aryl-H); δ C, 13.650 (2q, 2 × CH_3CH_2), 26.20 (t, C-7), 36.463, 37.798 (2t, C-6, and -9), 55.635 (s, C-8), 61.459 (2t, 2 × CH_2CH_3), 127.651, 128.559, 130.986, 132.442, 135.718, and 137.902 (m, aryl C), 170.781 (s, 2 ester C=O), and 204.398 (s, aryl C=O).

6-*Bromo*-8,8-*bisethoxycarbonyl*-6,7,8,9-*tetrahydrobenzocyclohepten*-5-*one* [6-*Bromo-derivative of* (9; R^1 = H)].—A solution of bromine in chloroform (6.50 cm^3; 3.0% v/v) was added dropwise to a vigorously stirred solution of the keto-diester (9; R^1 = H) (1.0 g, 3.29 mmol) in chloroform after which the reaction mixture was stirred for a further 15 min. After evaporation of the mixture to dryness the *product* (1.25 g, 99%) was obtained as a yellow-brown wax. Thick-layer chromatography (silica gel, MERCK 7747) with chloroform as eluant allowed isolation of an analytical sample. The product had b.p. 190 °C at 0.25 mmHg (Found: C, 53.65; H, 5.4; Br, 20.65. $C_{17}H_{19}BrO$ requires C, 53.3; H, 5.25; Br, 20.85%), $\nu_{max.}$ (film) 1 718 (ester C=O) and 1 689 cm^{-1} (aryl C=O); δ 1.1—1.43 (6 H, t, 2 × CH_3CH_2), 2.54—3.15 and 3.45 (4 H, m and dd, 7- and 9-CH_2), 4.0—4.35 (4 H, q, 2 × CH_2CH_3), 4.97 (1 H, dd, 6-H), 7.15—7.6, and 7.6—7.8 (4 H, m, aryl-H).

8-*Carboxy*-6,7,8,9-*tetrahydrobenzocyclohepten*-5-*one* (11; R^1 = H).—The keto-diester (9; R^1 = H) (1.35 g, 4.4 mmol) was refluxed with sodium hydroxide (0.35 g) in aqueous tetrahydrofuran (25 cm^3; 1 : 1 v/v) for 24 h after which it was concentrated under reduced pressure; concentrated hydrochloric acid was then added to it (until pH *ca.* 1). After further concentration under reduced pressure, the residue was shaken in ethanol–dichloromethane, and this, then filtered through a sintered-glass funnel, with thorough washing of the inorganic residue. The bulked liquors were then concentrated under reduced pressure (azeotroping traces of ethanol with water) to yield brown solids. These were then refluxed in aqueous sulphuric acid (50 cm^3; 3 : 1 v/v) for 4 h and left overnight at room temperature. The yellow-brown solid suspension was then collected and recrystallised from ethyl acetate to yield the product (0.65 g, 72%) as white *needles*, m.p. 131 °C (Found: C, 70.85; H, 6.2. $C_{12}H_{12}O_3$ requires C, 70.55; H, 5.9%), $\nu_{max.}$(KBr) 3 200—3 500br (OH), 1 700 (acid C=O), and 1 674 cm^{-1} (aryl C=O); δ 2.1 (2 H, q, 7-CH_2), 2.5—3.4 (5 H, m, 9-CH_2, 8-H, 6-CH_2), 7.2—7.6 (3 H, m, 1-, 2-, and 3-H), 7.67 (1 H, m, 4-H), and 11.60 (1 H, s, exchangeable, acid OH).

8-*Benzylcarbamoyl*-6,7,8,9-*tetrahydrobenzocyclohepten*-5-*one* (5; R^1 = R^2 = H, R^3 = $PhCH_2$).—(a) The acid (11; R^1 = H) (2.40 g, 11.8 mmol) was stirred with benzylamine (1.28 g, 11.9 mmol) in dichloromethane (40 cm^3) at 0 °C after which dicyclohexylcarbodi-imide (2.5 g, 12.1 mmol) was added in one portion in the same solvent (20 cm^3). The solution was allowed to reach room temperature after 30 min and, after a further 3.5 h, was filtered; the filtrate was concentrated under reduced pressure, filtered again, and finally evaporated to dryness under reduced pressure. A yellow solid was obtained, which consisted of 3 principal spots, none of which was assignable to starting material. Silica gel column chromatography (MERCK 7734) (500 g), with 33% ethyl acetate in cyclohexane as eluant, effected removal of dicyclohexylurea (high R_F), and then allowed isolation of a white crystalline material, which was the product (1.72 g, 50%). This was recrystallised from ethyl acetate to give white needles, m.p. 156 °C (Found: C, 77.8; H, 6.4; N, 4.75. $C_{19}H_{19}NO_2$ requires C, 77.8; H, 6.55; N, 4.75%); $\nu_{max.}$ (Nujol) 3 345 (NH), 1 665 (aryl C=O), and 1 650 cm^{-1} (amide C=O); δ 2.0 (2 H, m, 7-CH_2), 2.5—3.5 (5 H, m, 6- and 9-CH_2, 8-H), 4.28 (2 H, d, N-CH_2), 6.1 (1 H, br, t, exchangeable, NH), 7.1—7.5 (8 H, m, benzyl aryl -H and 1-, 2-, and 3-H), and 7.71 (1 H, dd, 4-H).

Another component of lower R_F was also isolated: N-(*carbonyl*-6,7,8,9-*tetrahydrobenzocyclohepten*-5-*one*)-N,N′-*dicylohexylurea* as a white solid (1.40 g, 29%), m.p. 121 °C (Found: C, 74.65; H, 8.6; N, 7.25. $C_{25}H_{34}N_2O_3$ requires C, 74.8; H, 8.8; N, 6.95%), $\nu_{max.}$ (Nujol) 3 380 (NH), 1 695, 1 682, 1 671, and 1 666 cm^{-1} (all C=O); δ 0.8—2.3 (22 H, m, cyclohexyl-CH_2 and 7-CH_2), 2.5—4.4 (7 H, m, 6- and 9-CH_2, 8-CH, cyclohexyl-CH), 6.25 (1 H, s, exchangeable NH), 7.17—7.60 (3 H, m, ary 1-, 2-, and 3-H), and 7.72—7.87 (1 H, m, 4-H).

(b) The acid (11; R = H) (5.95 g, 29.2 mmol) was stirred in dry acetonitrile (100 cm^3) with triethylamine (4.2 cm^3), then 2-chloro-1-methylpyridinium iodide (15 g) added. A solution of benzylamine (3.15 g) in acetonitrile (20 cm^3) was then added in one portion and stirring continued for a further 4 h. After removal of the solvent under reduced pressure followed by the addition of dichloromethane (*ca.* 80 cm^3) the reaction liquor was then washed with 6M-hydrochloric acid (4 × 50

cm^3), dilute sodium hydrogen carbonate (3 × 50 cm^3), and then water; it was then dried (Na_2SO_4), and evaporated under reduced pressure to give reddish yellow solids (7.30 g), which on trituration (ether) gave a yellow material (6.67 g, 78%). This was shown [spectroscopically and chromatographically (3% ethanol in dichloromethane)] to be identical to the product obtained in (a) above. Acidification and extraction (chloroform) of the sodium hydrogencarbonate washings allowed recovery of starting material (0.65 g, 11%).

8-Benzylcarbamoyl-6-bromo-6,7,8,9-tetrahydrobenzocyclohepten-5-one (5; R^1 = H, R^2 = Br, R^3 = $PhCH_2$).—The amide (5; R^1 = R^2 = H, R^3 = CH_2Ph) (0.50 g, 1.71 mmol) was stirred in glacial acetic acid (20 cm^3) after which bromine in acetic acid (2.93 cm^3, 3.0% v/v) was added dropwise during 5 min. After a further 15 min, the solvent was removed under reduced pressure (azeotroping traces of acetic acid with toluene) to leave a brown crystalline solid (0.635 g). Attempted recrystallisation (ethyl acetate) resulted in partial decomposition, as did silica-gel column chromatography [(MERCK 7734), with chloroform as eluant]. For this reason, material of analytical purity could not be obtained; C and Br analysis figures were consistently 1—2 and 2% in error, respectively [Found: C, 59.55; H, 4.75; Br, 23.5; N, 3.6. M^+, 291.1265 (−HBr from molecular ion). $C_{19}H_{18}BrNO_2$ requires C, 61.25; H, 4.85; Br, 21.45; N, 3.75%, *M*, 291.1259], $\nu_{max.}$ (Nujol) 3 270 (NH), 1 679 (aryl C=O), and 1 635 cm^{-1} (amide C=O); δ 2.3—3.3 (5 H, m, 7-, 9-CH_2 and 8-H), 4.35 [2 H, d (→s in D_2O), NCH_2], 4.82 and 5.02 [1 H (isomers), 2dd, 5-H], 7.1—7.7 (9 H, m, aryl), and 7.9 (1 H, br, d, exchangeable, NH).

3-Benzyl-1,2,3,4,5,6-hexahydro-2,5-methano-3-benzazocine-1,4-dione (12; R^1 = H, R^2 = $PhCH_2$).—The bromo-amides from above (1.55 g, 4.17 mmol) were refluxed in dry methanol (*ca.* 50 cm^3) with sodium methoxide [from 1.3 g sodium in excess methanol] for 3 h. The solvent was removed and water (50 cm^3) was added. After extraction (dichloromethane), followed by washing (water), drying (Na_2SO_4), and evaporation to dryness under reduced pressure the *product* (1.18 g, 97%) was obtained as an off-white solid. Recrystallisation from ethyl acetate–dichloromethane gave colourless rhombohedra, m.p. 122—123 °C (Found: C, 78.55; H, 6.05; N, 5.1%; M^+, 291.1275. $C_{19}H_{17}NO_2$ requires C, 78.75; H, 5.9; N, 4.8%; *M*, 291.1259), $\nu_{max.}$ (Nujol) 1 700 (lactam C=O), and 1 673 cm^{-1} (aryl C=O); δ 2.05 (1 H, d, *endo*-11-H), 2.60 (1 H, m, *exo*-11-H), 2.95 (1 H, m, 5-H), 3.2—3.5 (2 H, m, 6-CH_2), 4.1 (1 H, d, 2-H), 3.95 and 4.4 (2 H, 2d, N-CH_2), and 6.9—7.5 (9 H, m, aryl); δ_C 31.488 (t, C-11), 40.588 (d, C-5), 40.952 (t, C-6), 46.049 (t, Ph*C*), 66.495 (d, C-2), 127.651, 128.073, 128.986, 130.864, 131.777, 132.806, 135.417, and 135.781 (aryl-C), 176.305 (s, 4-C), and 204.639 (s, C-1).

3-Benzyl-1,2,3,4,5,6-hexahydro-2,5-methano-3-benzazocin-4-one (14; R^1 = H, R^2 = CH_2Ph).—The above keto-lactam (12; R^1 = H, R^2 = $PhCH_2$) (1.98 g, 6.8 mmol), potassium hydroxide (9.9 g), and hydrazine hydrate (17.0 cm^3, 100%) were stirred in digol (200 cm^3) for 1 h at 90—100 °C. After this period the condenser was removed, and the temperature then raised, such that the excess water was distilling from the reaction mixture. Once the temperature of the solution had reached *ca.* 170 °C (2—3 h), the condenser was replaced and the reaction mixture was refluxed for a further 2.5 h. The mixture was then cooled and poured onto ice–water (*ca.* 800 cm^3). The mixture was stirred (30 min) and filtered through a sintered glass funnel to give a white solid. This was then washed thoroughly with *concentrated* hydrochloric acid until only a grey gum remained. The latter was then washed into a separate container using dichloromethane and the resulting solution washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to give an off-white solid which recrystallised from light petroleum (b.p. 60—80 °C) as white needles (65%), m.p. 111—112 °C (Found: C, 82.45; H, 7.05; N, 5.2%); M^+, 277.1486. $C_{19}H_{19}NO$ requires C, 82.30; H, 6.9; N, 5.05%; *M*, 277.1467), $\nu_{max.}$ (Nujol) 1 689 and 1 670 cm^{-1} (C=O); δ 1.82 (1 H, d, *endo*-11-H), 2.4—2.7 (1 H, m, *exo*-11-H), 2.7—3.85 (5 H, m, 1- and 6-CH_2 and 5-H), 3.45 and 4.62 (2 H, 2d, NCH_2), 3.65—3.85 (1 H, m, 2-H), and 7.0—7.4 (9 H, m, aryl).

3-Benzyl-1,2,3,4,5,6-hexahydro-2,5-methano-3-benzazocine (1; R^1 = H, R^2 = $PhCH_2$).—The lactam (14; R^1 = H, R^2 = CH_2Ph) (2.0 g, 7.2 mmol) in dry tetrahydrofuran (THF) (30 cm^3) was added dropwise to a stirred suspension of lithium aluminium hydride (0.4 g) in THF (100 cm^3). The solution was then refluxed for 2.5 h, and, after being cooled, was diluted with water (0.5 cm^3), 15% aqueous sodium hydroxide (0.5 cm^3), and then water again (1.5 cm^3). The granular precipitate was then filtered off (Kieselguhr) and thoroughly washed with dichloromethane; the combined liquors were evaporated to dryness under reduced pressure. After the addition of dichloromethane, the solution was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to yield the product as an off-white *oil* (1.75 g, 92%), which was slightly unstable to air. Attempts to obtain analytical purity by distillation (b.p. 140 °C at 0.3 mmHg) were unsuccessful while column chromatography (silica gel, MERCK 7734), with 1% ethanol in chloroform as eluant led to material loss and partial decomposition (Found: C, 85.65; H, 8.05; N, 5.35%; M^+, 263.1629. $C_{19}H_{21}N$ requires C, 86.65; H, 8.05; N, 5.3%; *M*, 263.1674), δ 1.65 (1 H, d, *endo*-11-H), 2.3—3.0 (8 H, m, *exo*-11-H, 5-H, 1-, 6-, and 4-CH_2), 3.2—3.5 (1 H, m, 2-H), 3.47 and 3.73 (2 H, 2d, PhCH_2N), and 7.05—7.3 (9 H, m, aryl-H). The methiodide had m.p. 129—130 °C (Found: C, 58.45; H, 6.35; I, 31.0; N, 3.2. $C_{20}H_{24}IN$ requires C, 59.25; H, 6.35; I, 31.3, N, 3.45%).

3-Benzyl-1,2,3,4,5,6-hexahydro-1-hydroxy-2,5-methano-3-benzazocine (13).—The keto-lactam (12; R^1 = H; R^2 = CH_2Ph) (0.96 g, 3.28 mmol) in tetrahydrofuran (THF) (20 cm^3) was added dropwise to a stirred suspension of lithium aluminium hydride (1.3 g) in THF (100 cm^3). After being refluxed for 2.5 h, the mixture was cooled and then water (1.5 cm^3), 15% aqueous sodium hydroxide (1.5 cm^3), and water again (4.5 cm^3) were added to produce a granular precipitate. Filtration (Kieselguhr) and concentration of the liquors was followed by the addition of dichloromethane (*ca.* 50 cm^3) and then water (*ca.* 50 cm^3). The organic layer was separated, washed with water, dried (Na_2SO_4), and then concentrated under reduced pressure to give the product (0.78 g, 85%) as a colourless *oil* (2 : 1 diastereoisomeric mixture); this decomposed on attempted distillation. Column chromatography (0.51 g) (silica gel, MERCK 7734; 100 g), with 1% ethanol in dichloromethane as eluant, resulted in the isolation of a relatively pure sample; traces of polar material were, however, present in all fractions (Found: C, 81.15; H, 7.8; N, 4.9%; M^+, 279.1602. $C_{19}H_{21}NO$ requires C, 81.7; H, 7.6; N, 5.0%; *M*, 279.1623), $\nu_{max.}$ (film) 3 400br cm^{-1} (OH); δ 1.5 (1 H, d, *endo*-11-H), 1.9 (1 H, m, *exo*-11-H), 2.2—3.3 (6 H, m, 1 exchangeable, OH with 5-H, 4- and 6-CH_2), 3.4—3.7 (1 H, m, 2-H), 3.6—3.9 (2 H, 2d, PhCH_2N), 4.45—4.57 [1 H, 2d, $J_{1,2}$ 4.5 Hz and 6.5 Hz (isomers), 1-H], and 7.0—7.4 (9 H, m, aryl-H). The *methiodide* had m.p. 167—169 °C (decomp.) (Found: C, 57.25; H, 5.9; I, 30.0; N, 3.05. $C_{20}H_{24}INO$ requires C, 57.0; H, 5.75; I, 30.1; N, 3.3%).

Reaction of 3-Benzyl-1,2,3,4,5,6-hexahydro-2,5-methano-3-benzazocine-1,4-dione with Aluminium Chloride/Lithium

Aluminium Hydride.—To a stirred suspension of lithium aluminium hydride (0.22 g) in dry ether (40 cm^3) under nitrogen, was added in small portions, aluminium chloride (1.56 g). A solution/suspension of the ketoamide (12; R^1 = H; R^2 = CH_2Ph) (0.70 g, 2.41 mmol) in dry ether (20 cm^3) was then added in portions followed by ether (50 cm^3). After 3.5 h under reflux the solution was cooled, diluted with water (0.3 cm^3), 15% aqueous sodium hydroxide (0.3 cm^3) and water again (0.9 cm^3) and then filtered through Kieselguhr, the residue being washed thoroughly with dichloromethane. The filtrate was then concentrated under reduced pressure, and the residue redissolved in dichloromethane; this solution was then washed (water), dried (Na_2SO_4), and concentrated under reduced pressure to leave a colourless oil (0.56 g) which was shown spectroscopically to be identical with the amino-alcohol (13).

Diethyl 2-(m-*Methoxybenzyl*)*propanedioate* (6; R^1 = OMe).—This compound was prepared by the method of Hey and Nagdy.[9] In the hydrogenation step, the complete conversion of starting material could never be effected (maximum conconversion *ca.* 80%). This mixture was utilised in the next step as described below. Alternative catalysts used were, 10% palladium on charcoal and 5% platinum on charcoal.

Methyl 4,4-*Bisethoxycarbonyl*-5-(3-*methoxyphenyl*)*pentanoate* (7; R^1 = OMe).—The crude diester (6; R^1 = OMe) (12.5 g) was stirred overnight with methyl acrylate (2.7 g) and sodium hydride (0.020 g, 50% dispersion in oil). After the addition of dichloromethane, followed by washing (2M-hydrochloric acid then water), drying (Na_2SO_4), and concentration under reduced pressure, a colourless oil was obtained, which on distillation gave two components. The first (1.0 g) (b.p. 135 °C at 0.15 mmHg) was shown to be unsaturated diester from the first step above (n.m.r., i.r.) while the second (8.4 g) (b.p. 180 °C at 0.1 mmHg) was the *product* (74%) (Found: C, 62.4; H, 7.0. $C_{19}H_{26}O_7$ requires C, 62.3; H, 7.15%), $\nu_{max.}$ (film) 1 725—1 735br cm^{-1} (2 ethyl ester C=O, methyl ester C=O), δ 1.25 (6 H, t, 2 × CH_3CH_2), 2.28 (4 H, m, 2,3-CH_2), 3.22 (2 H, s, 5-CH_2), 3.66 (3 H, s, CO_2CH_3), 3.77 (3 H, s, aryl-OCH_3), 4.18 (4 H, q, 2CH_2CH_3), 6.61—6.88 (3 H, m, 4,5,6-aryl-H), and 7.18 (1 H, t, 2-H).

4,4-*Bisethoxycarbonyl*-5-(3-*methoxyphenyl*)*pentanoic Acid* (8; R^1 = OMe).—The triester (7; R^1 = OMe) (2.1 g, 5.9 mmol) was stirred at room temperature overnight with sodium hydroxide (0.23 g) in aqueous tetrahydrofuran (50 cm^3, 1 : 1 v/v). The mixture was then concentrated, diluted with water (*ca.* 50 cm^3) and the slight excess of unchanged starting material removed with toluene. Following the addition of concentrated hydrochloric acid to the aqueous layer, the free acid was extracted (dichloromethane) and the combined organic liquors were dried (Na_2SO_4) and concentrated under reduced pressure to yield the *product* (1.99 g, 95%). An analytical sample was obtained by distillation (b.p. 210 °C at 0.1 mmHg) (Found: C, 61.25; H, 7.05. $C_{18}H_{24}O_7$ requires C, 61.35; H, 6.85%), $\nu_{max.}$ (film) 3 050—3 500br (OH), 1 730 (ester C=O), and 1 710 cm^{-1} (acid C=O); δ 1.25 (6 H, t, 2 × CH_3CH_2), 2.30 (4 H, m, 2- and 3-CH_2), 3.25 (2 H, s, 5-CH_2), 3.65 (3 H, s, OCH_3), 4.2 (4 H, q, 2 × CH_2CH_3) 6.70—7.15 (4 H, m, aryl), and 10.68 (1 H, s, exchangeable OH).

8,8-*Bis*(*ethoxycarbonyl*)-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one* (9; R^1 = OMe).—(a) The acid (8; R^1 = OMe) (1.22 g, 3.65 mmol) was stirred with polyphosphoric acid (35 g) at 110—120 °C for 30 min after which it was cooled and poured onto ice–water (*ca.* 500 cm^3). After being stirred for 30 min the mixture was extracted with dichloromethane and the extract, washed (dilute aqueous sodium hydrogen carbonate and then water), dried (Na_2SO_4), and concentrated under reduced pressure to yield a dark brown gum. This, on distillation (b.p. 160 °C at 0.1 mmHg), gave a white waxy solid (0.57 g, 50%) which crystallised from light petroleum (b.p. 60—80 °C) as white needles, m.p. 70—71 °C (Found: C, 64.9; H, 6.7. $C_{18}H_{22}O_6$ requires C, 64.65; H, 6.65%), $\nu_{max.}$ (Nujol) 1 720 (ester C=O), 1 664 (aryl C=O), and 1 594 cm^{-1} (C ··· C); δ 1.3 (6 H, t, 2 × CH_3CH_2), 2.3 (2 H, m, 7-CH_2), 2.8 (2 H, m, 6-CH_2), 3.4 (2 H, s, 9-CH_2), 3.85 (3 H, s, OCH_3), 4.2 (4 H, q, 2CH_2CH_3), 6.8 (2 H, m, 1,3-H), and 7.75 (1 H, d, 4-H).

(b) The acid (1.36 g, 4.0 mmol) was stirred with methanesulphonic acid (8.0 g) and phosphorus pentoxide (1.5 g) for 36 h after which the mixture was diluted with water (30 cm^3) and stirred for 20 min. The mixture was extracted with dichloromethane and the extract dried (Na_2SO_4) and concentrated under reduced pressure to leave an off-white solid (0.94 g, 73%) which was shown (t.l.c., i.r., n.m.r.) to be identical with the keto-diester from (a) above.

8-*Carboxy*-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one* (11; R^1 = OMe).—The diester ketone (9; R = OMe) (2.54 g, 7.6 mmol) was stirred at room temperature for 40 h with sodium hydroxide (0.80 g) in aqueous tetrahydrofuran (75 cm^3, 1 : 1, v/v); concentrated hydrochloric acid was then added to the mixture (to pH 1) and the solvent removed under reduced pressure. The residue was shaken in ethanol–dichloromethane and the inorganic solids filtered off and thoroughly washed. The bulked liquors were then concentrated under reduced pressure (azeotroping traces of ethanol with water) to yield brown solids. These were then refluxed in aqueous sulphuric acid (100 cm^3, 3 : 1 v/v) for 4 h and left overnight at room temperature. The yellow-brown solid suspension was then filtered off (1.7 g) and recrystallised from ethyl acetate to yield the *product* (1.32 g, 74%), m.p. 152—153 °C. Spectroscopic data showed this to be identical with the acid (11; R^1 = OMe).[2]

6,7,8,9-*Tetrahydro*-8-*methoxycarbonyl*-2-*methoxycyclohepten*-5-*one* (4; R^1 = OMe, R^2 = H).—The mono-acid (11; R^1 = OMe) (1.25 g, 5.4 mmol) was refluxed in methanol (60 cm^3) with concentrated sulphuric acid (0.2 cm^3) for 3 h. The solvent was then removed and the residue shaken between dichloromethane (25 cm^3) and dilute sodium hydrogen carbonate solution (25 cm^3). The organic layer was separated, washed twice with water, dried (Na_2SO_4), and concentrated under reduced pressure to yield off-white solids which were then recrystallised from light petroleum (b.p. 60—80 °C) to give the product (1.21 g, 91%) as white *needles*, m.p. 57—58 °C (Found: C, 67.65; H, 6.3. $C_{14}H_{16}O_4$ requires C, 67.7; H, 6.5%), $\nu_{max.}$ (film) 1 725 (ester C=O) and 1 665 cm^{-1} (aryl C=O); δ 2.05(2H, br, dd, 7-CH_2), 2.65—3.3 (5 H, m, 9-CH_2, 8-CH, 6-CH_2), 2.71 (3 H, s, aryl-OCH_3), 2.82 (3 H, s, CO_2CH_3), 6.7—6.9 (2 H, m, 1- and 3-H), and 7.75 (1 H, d, 4 H).

6,7,8,9-*Tetrahydro*-2-*methoxy*-8-*methylcarbamoylbenzocyclohepten*-5-*one* (5; R^1 = OMe, R^2 = H, R^3 = Me).—(a) The mono-acid (11; R = OMe) (10.8 g, 47 mmol) was stirred in dry acetonitrile (150 cm^3) with triethylamine (7.2 cm^3) and then 2-chloro-1-methylpyridinium iodide (26 g) was added. A solution of methylamine (3.0 g) in acetonitrile (25 cm^3) was then added to the mixture in one portion. After the mixture had been stirred for 4 h the solvent was removed under reduced pressure and dichloromethane (150 cm^3) added. The reaction liquor was then washed with 6M-hydrochloric acid (4 × 50 cm^3), dilute aqueous sodium hydrogen carbonate (3 × 50 cm^3), and then water. After drying (Na_2SO_4), evaporation of the solution under reduced pressure yielded reddish solids, tritur-

ation of which with ether gave the product (7.3 g, 65%). Recrystallisation of this from ethyl acetate produced an analytical sample as fawn *platelets*, m.p. 156—157 °C (Found: C, 67.75; H, 7.0; N, 5.45. $C_{14}H_{17}NO_3$ requires C, 68.0; H, 6.95; N, 5.65%), $\nu_{max.}$ (Nujol) 3250, 3 180 (NH), 1 661 (aryl C=O), 1 628 (amide C=O) and 1 598 cm^{-1} (C ⋯ C); δ 2.0 (2 H, m, 7-CH_2), 2.5—3.45 (5 H, m, 9-CH_2, 8-H, 6-CH_2), 2.8 [3 H, d (collapse to s, with D_2O), CH_3N], 3.83 (3 H, s, CH_3O), 5.8—6.2 (1 H, br, s, exchangeable, NH), 6.65—6.85 (2 H, m, 1- and 3-H), and 7.75 (1 H, d, 4-H).

(b) The methyl ester (4; R^1 = OMe, R^2 = H, Et = Me) (1.23 g, 5.3 mmol) was left for 7 days in a saturated solution of methanolic methylamine (30 cm^3), after which time *ca.* 90% conversion to a product of low R_F had taken place [t.l.c. (4% ethanol in dichloromethane)]. Removal of the solvent under reduced pressure (traces of methylamine were azeotroped using benzene) left a yellowish solid (1.19 g) which was recrystallised from ethyl acetate as fawn platelets (0.87 g, 71%), m.p. 154—156 °C. These were shown spectroscopically to be identical with those obtained in (a) above.

(c) The preparation of the acid chloride (10; R^1 = OMe) from the acid (11; R^1 = OMe) (1.0 g, 4.3 mmol), which represents the first part of this procedure, is described above.

The freshly prepared crude acid chloride (10; R^1 = OMe) (0.98 g) in dry toluene (20 cm^3) was treated with a saturated solution of methylamine in dry toluene (25 cm^3) (added in several portions with vigorous stirring). After a further period (10 min) of stirring, the reaction mixture was washed with water, aqueous sodium hydrogen carbonate, and then water again; it was then dried (Na_2SO_4), concentrated under reduced pressure to give a reddish gum, which on crystallisation from ethyl acetate yielded fawn platelets (0.49 g, 46%), m.p. 154—156 °C. Spectroscopic evidence confirmed that this compound was identical with the amide product from (a).

6-Bromo-6,7,8,9-tetrahydro-2-methoxy-8-methylcarbamoylbenzocyclohepten-5-one (5; R^1 = OMe, R^2 = Br, R^3 = Me). —The amide (5; R^1 = OMe, R^2 = H, R^3 = Me) (6.54 g, 26.5 mmol) was stirred in glacial acetic acid (20 cm^3) and bromine in acetic acid (2.93 cm^3, 3.0% v/v) added slowly during 5 min. After a further period (15 min) of stirring, the solvent was removed under reduced pressure (azetroping remaining traces of acetic acid with toluene) to leave a brown crystalline solid (8.39 g), which, on t.l.c. (3% ethanol in dichloromethane) consisted of one major and two minor spots (two of which were, presumably, diastereoisomers). Attempted crystallisation resulted in decomposition and further purification was not attempted (Found: M^+, 325.0317, 327.0323. $C_{14}H_{16}BrNO_3$ requires *M*, 325.0314, 327.0294), $\nu_{max.}$ (Nujol) 3 300br (NH), 1 669 (aryl C=O), and 1 638 cm^{-1} (amide C=O); δ[$(CD_3)_2SO$] 2.0 (2 H, m, 7-CH_2), 2.55 [3 H, d (collapses to s in D_2O), CH_3N], 2.8—3.2 (3 H, m, 8-H and 9-CH_2), 3.8 (3 H, s, CH_3O), 3.8—4.2 (1 H, br, s, exchangeable, NH), 4.4 (1 H, dd, 6-H), 6.75—7.0 (2 H, m, 1-, and 3-H), and 7.70 (1 H, d, 4-H).

1,2,3,4,5,6-Hexahydro-8-methoxy-3-methyl-2,5-methano-3-benzazocine-1,4-dione (12; R^1 = OMe, R^2 = Me).—The bromo-amide (5; R^1 = OMe, R^2 = Br; R^3 = Me) (8.0 g, 24.5 mmol) was refluxed in dry methanol (*ca.* 50 cm^3) with sodium methoxide (from 2.7 g sodium in an excess of methanol) for 3 h. After removal of the solvent and addition of water (50 cm^3) to the mixture the organic materials were then washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to give yellowish solids. These upon trituration with ether gave the *product* as a pale yellow solid (4.9 g, 80%), an analytical sample of which was obtained upon recrystallisation from ethyl acetate–dichloromethane (colourless rhomboid plates), m.p. 142—143 °C (Found: C, 68.6; H, 6.2; N, 5.65. $C_{14}H_{15}NO_3$ requires C, 68.55; H, 6.15; N, 5.7%), $\nu_{max.}$ (Nujol) 1 705 (lactam C=O), 1 678 (aryl C=O), and 1 600 cm^{-1} (C ⋯ C); δ 2.16 (1 H, d, *endo*-11-H), 2.61 (3 H, s, CH_3N), 2.8—3.5 (4 H, m, *exo*-11-H, 5-H, 6-CH_2), 3.80 (3 H, s, CH_3O), 4.14 (1 H, d, 2-H), 6.6—6.9 (2 H, m, 7-H, and 9-H), and 7.75 (1 H, d, 10-H).

1,2,3,4,5,6-Hexahydro-8-methoxy-3-methyl-2,5-methano-3-benzazocin-4-one (14; R^1 = OMe, R^2 = Me).—The above keto-lactam (12; R^1 = OMe, R^2 = Me) (3.66 g, 14.9 mmol), potassium hydroxide (18.7 g), and hydrazine hydrate (36.9 cm^3, 100%) were stirred in digol (400 cm^3) for 1 h at 90—100 °C. After this period the condenser was removed and the temperature then raised to ensure that the excess of water was distilling from the reaction mixture. Once the temperature of the solution had reached *ca.* 170 °C (after 2—3 h), the condenser was replaced and the reaction mixture was refluxed for a further 2.5 h. The mixture was then cooled and poured onto ice–water (*ca.* 1.000 cm^3). After being stirred for 30 min the mixture was filtered through a sintered glass funnel to give a white solid which was washed thoroughly with concentrated hydrochloric acid until only a grey gum remained. This gum was dissolved in dichloromethane and the solution washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to provide an off-white solid, which was recrystallised from light petroleum (b.p. 60—80 °C) to give the product as white *platelets* (50%), m.p. 105 °C (Found: C, 72.55; H, 7.25; N, 6.05. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.4; N, 6.05%), $\nu_{max.}$ (Nujol) 1 688 and 1 672 cm^{-1} (C=O); δ 1.78 (1 H, d, *endo*-11-H), 2.48 (3 H, s, CH_3N), 2.05—3.40 (6 H, m, *exo*-11-H, 6-, 1-CH_2, 5-H), 3.7 (3 H, s, CH_3O), 3.65—3.90 (1 H, m, 2-H), 6.55—6.7 (2 H, m, 7- and 9-H), and 6.95 (1 H, d, 10-H).

1,2,3,4,5,6-Hexahydro-8-methoxy-3-methyl-2,5-methano-3-benzazocine (1; R^1 = OMe, R^2 = Me).—The lactam (14; R^1 = OMe, R^2 = Me) (1.42 g, 6.57 mmol) in tetrahydrofuran (THF) was added dropwise to a stirred suspension of lithium aluminium hydride (0.50 g) in THF (100 cm^3). After the mixture had been refluxed for 3 h it was cooled and water (0.5 cm^3), 15% sodium hydroxide solution (0.5 cm^3) and then water (1.5 cm^3) were added. The solution was filtered (Kieselguhr) and the precipitate was washed thoroughly with dichloromethane. The bulked washings were separated and the organic layer concentrated under reduced pressure; the residue was redissolved in dichloromethane. After washing (water) and drying (Na_2SO_4) of the solution, the solvent was removed under reduced pressure to leave the product as a colourless *oil* (1.20 g, 90%), b.p. 135 °C at 0.1 mmHg (Found: C, 76.75; H, 8.8; N, 6.65%; M^+, 216.1414. $C_{14}H_{19}NO$ requires C, 77.4; H, 8.8; N, 6.45%; *M*, 216.1388), $\nu_{max.}$ (film) 1 605 cm^{-1} (C=C); δ 1.65 (1 H, d, *endo*-11-H), 2.25 (3 H, s, CH_3N), 2.25—3.10 (8 H, m, *exo*-11-H, 5-H, 1-, 6-, and 4-CH_2), 3.2—3.45 (1 H, m, 2-H), 3.75 (3 H, s, CH_3O), 6.55—6.75 (2 H, m, 7- and 9-H), and 7.0, 7.25 (1 H, m, 10-H).

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References

1 Part 5, G. R. Proctor and F. J. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1754.
2 G. R. Proctor and F. J. Smith, *J. Chem. Res.*, 1980, (*S*), 286; (*M*) 3544.
3 R. Achini, *Helv. Chim. Acta*, 1981, **64**, 2203.
4 D. Caunt, W. D. Crow, R. D. Haworth, and C. A. Vodoz, *J. Chem. Soc.*, 1950, 1631.
5 G. N. Walker and D. Alkalay, *J. Org. Chem.*, 1966, **31**, 1905.

6 J. G. Cannon and J. P. Pease, *Org. Prep. Proced. Int.*, 1979, **11**, 63.
7 K. S. Kim, E. Vanotti, A. Suarato, and F. Johnson, *J. Am. Chem. Soc.*, 1979, **101**, 2483.
8 H. Leuchs, *Ber.*, 1911, **44**, 1507.
9 D. H. Hey and K. A. Nagdy, *J. Chem. Soc.*, 1953, 1894.
10 P. E. Eaton, G. R. Carlson, and J. T. Lee, *J. Org. Chem.*, 1973, **38**, 4071.
11 J. K. Sutherland and D. A. Widdowson, *J. Chem. Soc.*, 1964, 4650.
12 S. Shigematsu, Jap Patent 6363/1957 (*Chem. Abstr.*, 1958, **52**, 12916c).
13 R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, 1970, **35**, 4000.

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