Bridged-ring Nitrogen Compounds. Part 1. A Synthesis of a 2,3,4,5-Tetrahydro-1,4-ethano-1-benzazepin-5(1*H*)-one

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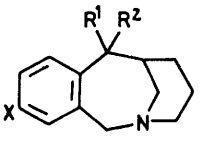
2,3,4,5-Tetrahydro-1,4-dimethyl-5-oxo-1-benzazepine has been obtained by methylation (MeI) of 2,3,4,5-tetrahydro-5-oxo-1*H*-1-benzazepine using lithium di-isopropylamide, but a similar attempted alkylation reaction with 1,2-di-iodoethane was unsuccessful. A synthesis of *N*-(3-methoxyphenyl)isonipecotic acid was developed from ethyl isonipecotate and dihydroresorcinol: the acid or its *O*-demethylated ethyl ester was cyclised in polyphosphoric acid at 180—190 °C yielding 2,3,4,5-tetrahydro-8-hydroxy-1,4-ethano-1-benzazepin-5(1*H*)-one. Syntheses of perhydro-1-(*m*-methoxyphenyl)azocin-5-one and perhydro-1-(*p*-tolylsulphonyl)azocin-5-one are described.

DERIVATIVES of the 2,3,4,5,6,7-hexahydro-2,6-methano-2-benzazonine system (1; $R^1 = R^2 = X = H$) are unknown and we were interested in the possibility that the 7-keto-derivatives (1; R^1, $R^2 = O$, X = H or OMe) might be obtained by either Dieckmann cyclisation of amino-diesters [*e.g.* (2)] or by intramolecular Friedel–Crafts cyclisation of amino-acids [*e.g.* (3; R = H, OMe)]. The starting materials [(2) and (3)], made by conventional procedures (see Experimental section), were repeatedly subjected to the appropriate conditions for cyclisation but in no case were these successful. While this work was in progress we discovered [1] that the related amino-ketones (4; R = H, Me) were very unstable as free bases and concluded that it was pointless to continue attempts to make the amino-ketones (1; R^1, $R^2 = O$).



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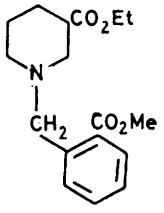

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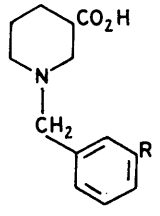

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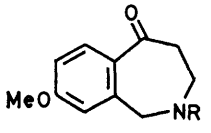

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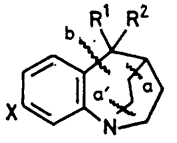

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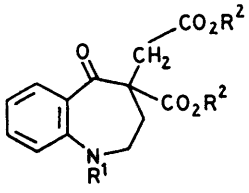
An alternative target, which does not involve working with Mannich bases, is the 1,4-ethano-1-benzazepine system (5; $R^1 = R^2 = H$). Access to the 5-keto-derivatives (5; R^1, $R^2 = O$) of this system seemed possible from 2,3,4,5-tetrahydro-1-benzazepin-5-ones previously made by us,[2] for example *via* bond fissions a and a′ (5).

RESULTS AND DISCUSSION

The diacid [2] (6; R^1 = tosyl, $R^2 = H$) could not be cyclised with Lewis acids to give a bridged amide, but it could be detosylated to (6; $R^1 = R^2 = H$) and re-esterified to (6; $R^1 = H$, $R^2 = Et$). However, when the latter was treated with sodium hydride in DMF (*cf.* ref. 3), no useful products were found.

Recent work on formation of dicarbanions using lithium di-isopropylamide [4,5] suggested that the 2,3,4,5-tetrahydro-1-benzazepin-5-one (7; R = H) might react



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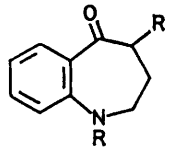
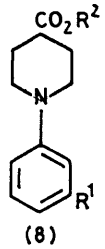


(7)

with this reagent to give the dianion (7; R = negative charge). This expectation was fulfilled and the dianion was alkylated with methyl iodide in 70% yield giving the disubstituted product (7; R = Me). However, the dianion reacted with 1,2-di-iodoethane to give an intractable mixture not including the bridged ketone (5; X = H, R^1, $R^2 = O$), which it was hoped might be formed.

To investigate an alternative cyclisation mode (*via* bond fission b) it was necessary to obtain the 1-aryl-piperidine-4-carboxylates (1-arylisonipecotates) (8). Although the keto-ester (9; R = CO_2Et) could be obtained



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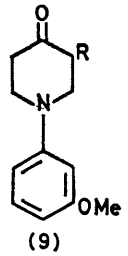

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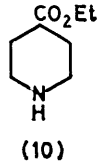

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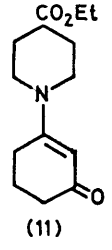
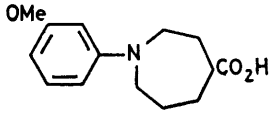


(11)

by a classical procedure, its hydrolysis to the corresponding piperidine (9; R = H) was unsuccessful, apparently due partly to retro-Michael reactions. While benzyne

has been caused to react with piperidine [6] to give *N*-phenylpiperidine, we found that, not surprisingly, this procedure did not apply usefully to ethyl isonipecotate (ethyl piperidine-4-carboxylate) (10). Accordingly a novel approach was adopted: ethyl isonipecotate (10) was reacted with dihydroresorcinol to give the enamino-keto-ester (11) which was dehydrogenated quite efficiently with 30% palladium–charcoal in boiling mesitylene to give the hydroxy-ester (8; R^1 = OH, R^2 = Et). The latter was methylated and hydrolysed yielding the amino-acid (8; R^1 = OMe, R^2 = H) which was cyclised with polyphosphoric acid at 180—190 °C to provide 8% of a hydroxy-amino-ketone ($C_{12}H_{13}NO_2$) which we believe has structure (5; X = OH, R^1,R^2 = O) for the following reasons. The mass spectrum showed not only the molecular ion but an $[M - CO]^+$ ion; the ^{1}H n.m.r. spectrum was in accord with the structure given and the ^{13}C n.m.r. spectrum revealed ten different kinds of carbon atoms including two identical pairs. A pK_a determination [7] gave values of 5.4 ± 0.3 and 9.5 ± 0.25; the second value is attributable to the phenolic hydroxy group, while the first has to be due to the bridgehead nitrogen. Contrastingly the parent substance 2,3,4,5-tetrahydro-1-benzazepin-5-one [2] had a pK_a of 2.5 ± 0.2. So it is concluded that introduction of the bridge (CH_2CH_2) from the nitrogen atom to C-4 increased the basicity of the nitrogen atom by a factor of *ca.* 10^3. Models indicate that overlap of the nitrogen *p*-electrons with the π-electron cloud of the ring is severely restricted.

Many unsuccessful attempts were made to improve the yield of the ketone (5; X = OH, R^1, R^2 = O), however, it was found that the hydroxy-ester (8; R^1 = OH, R^2 = Et) also cyclised in 8% yield thus significantly shortening the synthesis. The poor yield may be due in some degree to the energy required to flip the piperidine ring from a chair to a boat form, as pointed out by May.[8] Since a saturated seven-membered ring is more flexible we sought ways to obtain amino-acids of that ring size [*e.g.* 12)]. Attempts to obtain the amino-ketone (13)



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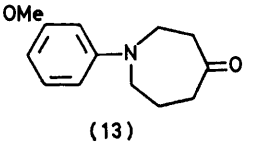

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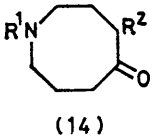

(14)

via the Dieckmann cyclisation followed by hydrolysis were entirely unsuccessful but the higher homologue (14; R^1 = *m*-methoxyphenyl, R^2 = CO_2Et) was made and hydrolysed to the ketone (14; R^1 = *m*-methoxyphenyl, R^2 = H). It was intended to convert the latter to the desired acid (12) either by Favorski reaction or by treatment with thallium(III) nitrate [9] but neither approach was successful. During this work, the *N*-tosyl β-keto-ester (14; R^1 = tosyl, R^2 = CO_2Et) and ketone (14; R^1 = tosyl, R^2 = H) were made for comparison. It was noticed that, except at the highest dilution, the Dieckmann cyclisation produced an intermolecular condensation product (presumably a 16-membered ring) along with the keto-ester (14; R^1 = *m*-methoxyphenyl, R^2 = CO_2Et).

EXPERIMENTAL

Quaternary Salts from Ethyl Nicotinate.—The appropriate bromide was heated with ethyl nicotinate in anhydrous methanol and the solvent was removed to allow recrystallisation from anhydrous acetone. The following products were thus obtained: (*a*) from methyl *o*-bromomethylbenzoate,[10] the product had m.p. 81—82 °C (Found: C, 54.35; H, 4.85; N, 3.4. $C_{17}H_{18}BrNO_4 + C_3H_6O$ requires C, 54.85; H, 5.5; N, 3.2%); (*b*) from benzyl bromide the product had m.p. 137—138.5 °C (Found: C, 55.55; H, 4.7; N, 4.3. $C_{15}H_{16}BrNO_2$ requires C, 55.5; H, 5.0; N, 4.35%); (*c*) from *m*-methoxybenzyl bromide the product had m.p. 93—95 °C (Found: N, 3.6; Br, 22.65. $C_{16}H_{18}BrNO_3$ requires N, 4.0; Br, 22.7%); (*d*) from ethyl γ-bromobutyrate a gum was obtained and used as such.

Hydrogenation of Ethyl Nicotinate Quaternary Salts.—These were hydrogenated over platinum oxide in acetic acid. The following products were obtained from the appropriate salts referred to above: (a) ethyl *N*-(*o*-methoxycarbonylbenzyl)nipecotate (2), b.p. 150—152 °C at 0.3 mmHg (Found: C, 66.6; H, 7.55; N, 4.75. $C_{17}H_{23}NO_4$ requires C, 66.85; H, 7.6; N, 4.6%); τ 2.2—2.8 (4 H, m, aryl), 5.9 (2 H, q, CH_2CH_3), 6.12 (3 H, s, *Me*), 6.25 (2 H, s, CH_2Ph), 7.1—8.7 (9 H, m, piperidine ring), and 8.82 (3 H, t, CH_3CH_2); (*b*) ethyl *N*-benzylnipecotate [ethyl ester of (3; R = H)], b.p. 116—118 °C at 0.3 mmHg (lit.,[11] b.p. 113—117 °C) (Found: C, 72.95; H, 8.55; N, 5.3. Calc. for $C_{15}H_{21}NO_2$: C, 72.85; H, 8.55; N, 5.65%); τ 2.67 (5 H, s, aryl), 5.9 (2 H, q, CH_2CH_3), 6.5 (2 H, s, CH_2Ph), 7.0—8.6 (9 H, m, piperidine ring), and 8.8 (3 H, t, CH_3CH_2); (*c*) ethyl *N*-(*m*-methoxybenzyl)nipectate [ethyl ester of (3; R = OMe)], b.p. 145 °C at 0.3 mmHg (Found: C, 69.0; H, 8.3; N, 5.35. $C_{16}H_{23}NO_3$ requires C, 69.3; H, 8.35; N, 5.05%); τ 2.65—3.25 (4 H, m, aryl), 5.9 (2 H, q, CH_2CH_3), 6.2 (3 H, s, OMe), 6.5 (2 H, s, CH_2Ph), 7.0—8.65 (9 H, m, piperidine ring), and 8.8 (3 H, t, CH_3CH_2); (*d*) ethyl *N*-(3-ethoxycarbonylpropyl)nipecotate, b.p. 110—120 °C at 0.2 mmHg (Found: C, 62.05; H, 9.2; N, 5.3. $C_{14}H_{25}NO_4$ requires C, 61.95; H, 9.3; N, 5.15%); τ 5.84 (4 H, q, 2 CH_2CH_3), 7.0—8.6 (15 H, m, various CH_2), and 8.75 (6 H, t, 2 CH_2CH_3).

Ethyl 4-Ethoxycarbonylmethyl-2,3,4,5-tetrahydro-5-oxo-1H-1-benzazepine-4-carboxylate (6; R^1 = H, R^2 = Et).—4-Carboxymethyl-2,3,4,5-tetrahydro-5-oxo-1-tosyl-1*H*-1-benzazepine-4-carboxylate [2] (6; R^1 = tosyl, R^2 = H) (1.36 g) was stirred for 27 h at 50 °C with sulphuric acid (40% v/v) [12] in acetic acid (10 ml). After addition to ice, the reaction mixture was extracted with chloroform, adjusted to pH 7 with sodium hydroxide and evaporated *in vacuo*. The residue was extracted with hot ethanol to give *4-carboxymethyl-2,3,4,5-tetrahydro-5-oxo-1H-1-benzazepine-4-carboxylic acid* (550 mg), m.p. 202—204 °C (Found: C, 47.3; H, 3.6; N, 4.15. $C_{13}H_{13}NO_5 \cdot 0.5Na_2SO_4$ requires C, 47.15; H, 3.95; N, 4.25%). The latter was refluxed for 8 h with ethanol containing a few drops of concentrated

sulphuric acid to yield the desired *product* (50%) as a gum purified by preparative t.l.c. [Found: C, 63.6; H, 6.6; N, 4.25%. M^+, 319.138 8 (100%). $C_{17}H_{21}NO_5$ requires C, 64.0; H, 6.65; N, 4.4%; *M*, 319.142 0]; τ 2.2—2.9 (4 H, m, aryl), 2.8 (1 H, exchangeable, NH), 5.85 (4 H, q, 2 CH_2CH_3), 6.2—6.3 (2 H, dd, CH_2CO_2Et), 7.0—7.22 (2 H, m, CH_2N), 7.45—7.65 (2 H, m, 3-H), and 8.7 and 8.8 (6 H, 2 t, 2 CH_3CH_2).

1,2,3,4-*Tetrahydro*-1,4-*dimethyl*-1-*benzazepin*-5-*one* (7; R = Me).—Di-isopropylamine (1 ml) and butyl-lithium in hexane (5 ml of 15% w/w) were reacted [4] at 0 °C in dry THF (10 ml) at 0 °C. After cooling to −78 °C, 1,2,3,4-tetrahydro-1-benzazepin-5-one [2] (440 mg) in dry THF (8 ml) was added dropwise whereupon an orange suspension was formed. After 30 min at −78 °C, methyl iodide (0.35 ml), hexamethylphosphoramide [4] (0.61 ml), and dry THF (5 ml) were added. After 1 h at −78 °C, the stirred reaction mixture was warmed to 20 °C during 1 h and set aside overnight. Work-up [4] gave the *product* (400 mg) purified by preparative t.l.c.: it had b.p. 85 °C at 0.05 mmHg [Found: C, 76.45; H, 8.05; N, 7.55%; M^+, 189.112 8 (100%). $C_{12}H_{15}NO$ requires C, 76.25; H, 8.0; N, 7.4%; *M*, 189.115 4]; τ 2.2—3.4 (4 H, m, aryl), 6.9 (3 H, s, NMe), 6.6—8.6 (5 H, m, 2-, 3-, and 4-H), and 8.86 (3 H, d, CH_3CH). When 1,2-di-iodoethane was used in the above reaction, several products were obtained including a yellow crystalline unstable substance (which liberated iodine), m.p. 107 °C, of approximate composition $C_{12}H_{14}$-INO.

The Enamine (11) *of Ethyl Isonipecotate and Dihydroresorcinol*.—Dihydroresorcinol (11 g), ethyl isonipecotate (10) (15 g), and dry benzene (180 ml) were refluxed for 6 h using a water separator. After removal of solvent, the residue (24 g) was distilled from a horizontal tube (Kugelrohr), b.p. 155—160 °C at 0.1 mmHg as a yellow oil (20 g) [Found: C, 66.4; H, 8.4; N, 5.3%, M^+ 251.152 0 (100%). $C_{14}H_{21}NO_3$ requires C, 67.0; H, 8.45; N, 5.6%; *M* 251.152 1]; $\nu_{max.}$ (film) 1 720 (CO_2Et) and 1 610 (CO) cm^{-1}: τ 4.85 (1 H, s, exchangeable slowly, vinylic H), 5.96 (2 H, q, CH_2CH_3), 6.2—6.45 and 6.9—8.45 (15 H, m, ring CH_2 and CH), and 8.8 (3 H, t, CH_3CH_2).

Ethyl N-(3-*Hydroxyphenyl*)*isonipecotate* (8; R^1 = OH, R^2 = Et).—The previous enamine (5 g), 10% Pd–C (1 g), and mesitylene (35 ml) were refluxed and stirred for 3 h at 170 °C. After removal of solvent *in vacuo*, the residue was chromatographed on silica and distilled in a Kugelrohr tube, yield 40%, b.p. 165 °C at 0.05 mmHg (Found: C, 66.65; H, 7.8; N, 5.65. $C_{14}H_{19}NO_3$ requires C, 67.2; H, 7.9; N, 5.6%).

Ethyl N-(3-*Methoxyphenyl*)*isonipecotate* (8; R^1 = OMe, R^2 = Et).—The crude dehydrogenation product from above (10 g) was stirred under nitrogen in dry DMF (50 ml) with sodium hydride (80%; 2 g) for 2 h at 60 °C. After cooling, methyl iodide (10 g) was added and the mixture was stirred overnight. The usual work-up gave the product (5 g), b.p. 138—142 °C at 0.1 mmHg as a pale yellow oil (Found: C, 68.5; H, 8.05; N, 4.85%; M^+, 263.150 0. $C_{15}H_{21}NO_3$ requires C, 68.5; H, 8.05; N, 5.3%; *M*, 263.152 1); $\nu_{max.}$ (film) 1 720 cm^{-1} (CO_2Et); τ 3.0—3.85 (4 H, m, aryl-H), 5.98 (2 H, q, CH_2CH_3), 6.32 (3 H, s, OMe), 6.38—6.42 and 7.2—8.3 (9 H, m, ring CH_2 and CH), and 8.8 (3 H, t, CH_3CH_2).

N-(3-*Methoxyphenyl*)*isonipecotic Acid* (8; R^1 = OMe, R^2 = H).—The usual sodium hydroxide hydrolysis of the ester (2.05 g) from the preceding preparation gave the *product* (1.75 g) which crystallised from dichloromethane–light petroleum (b.p. 60—80 °C) as a cream powder, m.p. 105 °C (Found: C, 66.75; H, 7.3; N, 6.25. $C_{13}H_{17}NO_3$ requires C, 66.45; H, 7.3; N, 5.95%): τ −1.25 (1 H, exchangeable, O*H*), 2.9—3.8 (4 H, m, aryl-H), 6.3 (3 H, s, OMe), and 6.3—6.5 and 7.1—8.3 (9 H, m, ring CH_2 and CH).

1,2,3,4-*Tetrahydro*-8-*hydroxy*-1,4-*ethano*-1H-1-*benzazepin*-5-*one* (5; X = OH, R^1, R^2 = O).—*N*-(3-Methoxyphenyl)-isonipecotic acid (4 g) and polyphosphoric acid (150 g) were stirred at 180—190 °C for 20 h. After cooling the reaction mixture, it was poured into ice, adjusted to pH 7 and extracted exhaustively with chloroform to yield 615 mg of material which was purified by chromatography on silica and by distillation, b.p. 105—110 °C at 0.05 mmHg, yield 275 mg (7.5%), m.p. 78—80 °C [Found: C, 71.35; H, 6.8; N, 6.6%; M^+, 203.095 0 (100%). $C_{12}H_{13}NO_2$ requires C, 71.0; H, 6.45; N, 6.9%; *M*, 203.094 6]; $\nu_{max.}$ (CCl_4) 3 400—3 200 (OH) and 1 660 (CO) cm^{-1}; τ −2.36 (1 H, exchangeable, OH), 2.7—3.45 (3 H, m, aryl-H), 6.6—7.25 (5 H, m, ring CH_2 and CH), and 8.0—8.3 (4 H, m, ring CH_2). ^{13}C N.m.r. showed ten peaks: δ 210.5, 164.0, 157.6, 136.2, 120.0, 119.7, 115.9, 48.3(2), 46.9, and 23.9(2). Using a u.v. procedure,[7] at 550 nm the following pK_a values were obtained (pH in parentheses); 5.07 (3.7), 5.26 (4.8), 5.53 (5.25), 5.79 (5.63), 6.66 (6.69), 9.44 (9.9), 9.58 (10.29), and 9.57 (10.66).

Ethyl 4-[N-(3-*Ethoxycarbonylpropyl*)-3-*methoxyanilino*]-*butanoate*.—*m*-Anisidine (5 g), ethyl γ-bromobutyrate (19.7 g), freshly roasted potassium carbonate (21 g), and AnalaR acetone (250 ml) were stirred at 65 °C for 7 d. Chromatography of the crude product on neutral alumina (10% ether–benzene) yielded first the *product* (1.6 g), b.p. 170 °C at 0.01 mmHg (Found: C, 64.55; H, 8.0; N, 4.3. $C_{19}H_{29}NO_5$ requires C, 64.95; H, 8.3; N, 4.0%); $\nu_{max.}$ (film) 1 730 (ester) cm^{-1}; τ 2.8—3.0 (1 H, m, aryl-H), 3.6—3.85 (3 H, m, aryl-H), 5.88 (4 H, q, CH_2CH_3), 6.25 (3 H, s, OMe), 6.7 (4 H, t, CH_2N), 7.7 (4 H, t, CH_2CO_2Et), 7.97—8.25 (4 H, m, $CH_2CH_2CH_2$), and 8.78 (6 H, t, CH_3CH_2). The second product eluted was *ethyl* 4-(3-*methoxyanilino*)-*butanoate* (0.95 g), b.p. 145 °C at 0.02 mmHg (Found: C, 66.4; H, 8.05; N, 5.7. $C_{13}H_{19}NO_3$ requires C, 65.85; H, 8.05; N, 5.9%); $\nu_{max.}$ (film) 3 400 (NH) and 1 730 (ester) cm^{-1}; τ 2.8—3.05 (1 H, m, aryl-H), 3.68—3.9 (3 H, m, aryl-H), 5.88 (2 H, q, CH_2CH_3), 6.22 (1 H, exchangeable, NH), 6.28 (3 H, s, OMe), 6.88 (2 H, t, CH_2CO_2Et), 7.6 (2 H, t, CH_2N), 7.9—8.22 (2 H, m, $CH_2CH_2CH_2$), and 8.78 (3 H, t, CH_3CH_2). It was possible to avoid production of the latter compound by conducting the experiment at 110 °C and by adding an additional quantity (10 g) of ethyl γ-bromobutyrate after 3 d: in this case the yield of the pure desired material was 56% without chromatography.

Perhydro-1-(3-*methoxyphenyl*)*azocin*-5-*one* (14; R^1 = m-*methoxyphenyl*, R^2 = H).—Ethyl 4-[*N*-(3-ethoxycarbonylpropyl)-3-methoxyanilino]butanoate (43.5 g) in toluene (1 l) was added dropwise during 24 h to potassium t-butoxide [from potassium (14.3 g)] in toluene (1 l) with stirring at 120 °C. After slow distillation to b.p. 110 °C, the reaction mixture was cooled and worked-up as usual. The crude keto-ester (32 g) was refluxed for 48 h with acetic acid (240 ml), concentrated hydrochloric acid (40 ml), ethanol (80 ml), and water (40 ml). After cooling and basification, extraction with chloroform gave a gum (20 g) which was chromatographed on alumina and on silica. Elution removed first 400 mg of *dimeric product* (16-membered ring?) (from EtOH), m.p. 119—119.5 °C

[Found: C, 72.1; H, 7.85; N, 6.15%; *M* (osmometry), 448. $C_{28}H_{38}N_2O_4$ requires C, 72.05; H, 8.2; N, 6.0%; *M*, 466]; $\nu_{max.}$ (Nujol) 1 710 (CO) cm^{-1}; τ 2.8—3.05 (2 H, m, aryl-H), 3.65—3.9 (6 H, m, aryl-H), 6.28 (6 H, s, OMe), 6.8 (8 H, t, 4 CH_2CO), 7.61 (8 H, t, 4 CH_2N), and 8.0—8.3 (8 H, m, 4 $CH_2CH_2CH_2$). Second the *product* (12 g) (from ethanol) was eluted, m.p. 97—98 °C [Found: C, 71.5; H, 8.05; N, 5.65%; *M* (osmometry) 228. $C_{14}H_{19}NO_2$ requires C, 72.05; H, 8.2; N, 6.0%; *M*, 233]; $\nu_{max.}$ (Nujol) 1 690 cm^{-1} (CO): τ 2.85—3.05 (1 H, m, aryl-H), 3.65—3.85 (3 H, m, aryl-H), 6.3 (3 H, s, OMe), 7.73 (4 H, t, 2 CH_2CO), and 7.6—8.03 (8 H, m, 2 CH_2CH_2N).

1-[2(?)-*Bromo-5-methoxyphenyl*]-*perhydroazocin-5-one* (14; R^1 = 2-*bromo-5-methoxyphenyl*).—Perhydro-1-(*m*-methoxyphenyl)-5-oxoazocine (1.16 g), potassium carbonate (6 g), chloroform (100 ml), and bromine (0.5 ml) were stirred at 0 °C for 1 h and at 20 °C for 2 h, and then filtered and the filtrate evaporated. The residue was chromatographed on silica gel and crystallised from ether. The product had m.p. 113—114 °C (Found: C, 53.75; H, 5.8; N, 4.5. $C_{14}H_{18}BrNO_2$ requires C, 53.9; H, 5.8; N, 4.5%); τ 2.67—2.8 (1 H, m, aryl-H), 3.72—3.9 (2 H, m, aryl-H), 6.17 (3 H, s, OMe), 6.7 (4 H, t, CH_2N), and 7.55—8.0 (8 H, m, various CH_2).

Ethyl 4-[N-(3-*ethoxycarbonylpropyl*)-p-*tolylsulphonamido*]-*butanoate*.—Toluene-*p*-sulphonamide (8 g), ethyl γ-bromobutyrate (24.5 g), potassium carbonate (35 g, freshly roasted), and dry acetone (120 ml) were stirred and refluxed for 2 d. After cooling and filtration, the usual work-up yielded a pale yellow oil which was purified by chromatography on neutral alumina (yield 16 g) (Found: C, 57.7; H, 7.5. $C_{19}H_{29}NO_6S$ requires C, 57.2; H, 7.35%); $\nu_{max.}$ (film) 1 725 (CO_2Et) cm^{-1}; τ 2.35 (2 H, d, *J* 9 Hz, aryl-H), 2.74, (2 H, d, *J* 9 Hz, aryl-H), 5.92 (4 H, q, 2 OCH_2CH_3), 6.87 (4 H, t, 2 CH_2CO_2Et), 7.63 (3 H, s, Me), 7.7 (4 H, t, 2 CH_2NTos), 8.0—8.34 (4 H, m, 2 $CH_2CH_2CH_2$), and 8.78 (6 H, t, 2 CH_3CH_2).

4-*Ethoxycarbonylperhydro*-1-(p-*tolylsulphonyl*)*azocin-5-one* (14; R^1 = *tosyl*, R^2 = CO_2Et).—The above diester (6.7 g) was treated with potassium t-butoxide [from potassium (2.05 g)] in dry toluene (600 ml) as described previously. The *product* (1.5 g) crystallised from ethanol as needles, m.p. 110—112 °C (Found: C, 57.6; H, 6.5; N, 3.9. $C_{17}H_{23}NSO_5$ requires C, 57.75; H, 6.55; N, 3.95%); $\nu_{max.}$ (Nujol) 1 752 (ester) and 1 714 (CO) cm^{-1}; τ 2.4 (2 H, d, *J* 9 Hz, aryl-H), 2.75 (2 H, d, *J* 9 Hz, aryl-H), 5.9 (2 H, q, CH_2CH_3), 6.46 (1 H, dd, $CHCO_2Et$), 6.7—7.2 (4 H, m, ring CH_2), 7.6 (3 H, s, Me), 7.3—8.25 (6 H, m, ring CH_2), and 8.8 (3 H, t, CH_3CH_2).

Perhydro-1-(p-*tolylsulphonyl*)*azocin-5-one* (14; R^1 = *tosyl*, R^2 = H).—4-Ethoxycarbonylperhydro-1-(*p*-tolylsulphonyl)azocin-5-one (12 g) was refluxed for 48 h in acetic acid (72 ml), concentrated hydrochloric acid (12 ml), water (12 ml), and ethanol (24 ml). The *product* (8.9 g) was recrystallised from ethanol as buff microcrystals, m.p. 152—153 °C (Found: C, 59.65; H, 6.75; N, 4.55. $C_{14}H_{19}NO_3S$ requires C, 59.85; H, 7.15; N, 5.0%); $\nu_{max.}$ (Nujol) 1 690 cm^{-1} (CO); τ 2.5 (2 H, d, *J* 10 Hz, aryl-H), 2.85 (2 H, d, *J* 10 Hz, aryl-H), 7.0 (4 H, t, 2 CH_2CO), 3.58—3.78 (4 H, m, 2 CH_2N), 7.65 (3 H, s, CH_3), and 8.8—9.1 (4 H, m, 2 $CH_2CH_2CH_2$).

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