Synthesis of 2,3,4,4a,9,9a-Hexahydro-3,9-methano-1*H*-indeno[2,1-*c*]pyridine and Some *N*-Substituted Derivatives

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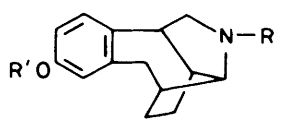
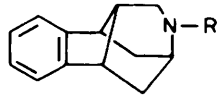
The construction of the very rigid 2,3,4,4a,9,9a-hexahydro-3,9-methano-1*H*-indeno[2,1-*c*]pyridine system by three different routes is presented. One of the routes led also to another novel azabenzotricyclodecane system, *viz.* to the compound 2-(*p*-tolylsulphonyl)-1,2,3,3a,8,8a-hexahydro-3,8-ethanoindeno[1,2-*c*]pyrrole, which was the result of a skeletal rearrangement. The last of the routes gives easy access to the title compound and its derivatives.

After syntheses of some derivatives of 1,2,3,4,5,6-hexahydro-5,1,4-propan[1]yl[3]ylidene-3-benzazocine (**1**),[1] our efforts were directed towards the preparation of another very rigid azabenzotricycloalkane, namely 2,3,4,4a,9,9a-hexahydro-3,9-methano-1*H*-indeno[2,1-*c*]pyridine (**2**).



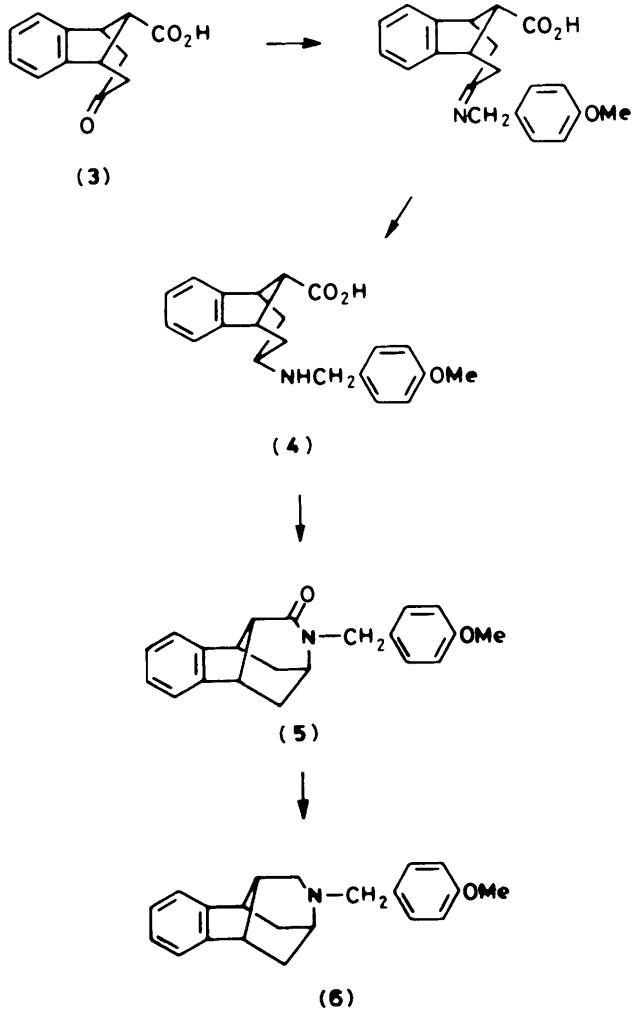
(**1**)



(**2**)

The obvious starting material for synthetic work in this area was the known oxo acid (**3**) (Scheme 1) which is made in three steps from *o*-phthalaldehyde.[2] Reduction of this oxo acid (**3**) with sodium borohydride gives the lactone of the *cis*-hydroxy acid in a slow, but quite high yielding, reaction.[2] On this basis the reductive amination of compound (**3**) with 4-methoxybenzylamine and sodium cyanoborohydride was tried. This reaction was extremely slow (10 days) but did give the desired 4-methoxybenzylamino carboxylic acid (**4**) in acceptable yield and with the correct geometry as shown by its thermal cyclization to the lactam (**5**). The latter was reduced with lithium aluminium hydride to provide the tertiary amine (**6**).

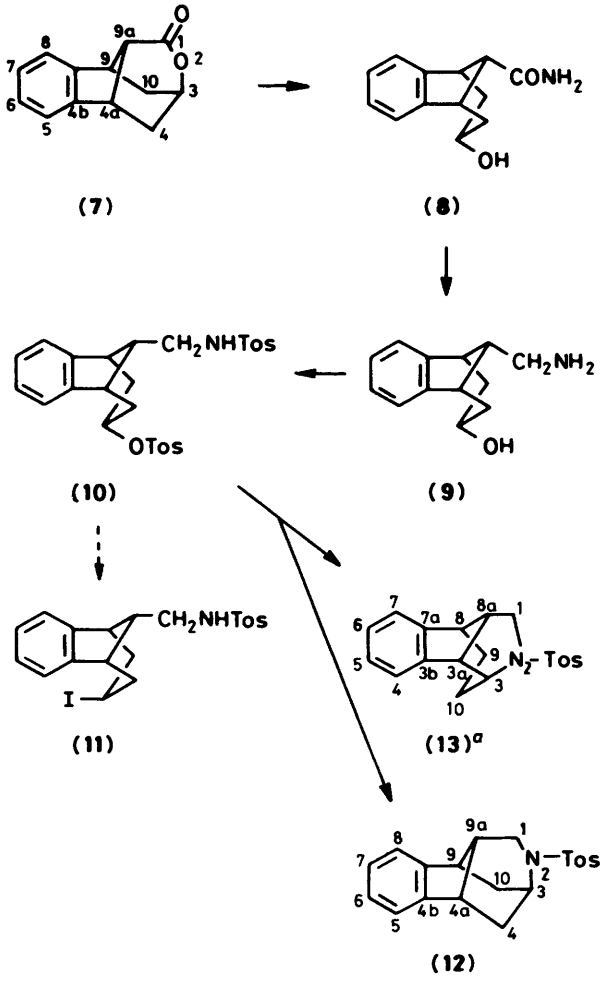
Although the above route is probably fairly general, a more convenient synthesis was sought, and the readily available lactone (**7**)[2] (Scheme 2) seemed an appropriate starting material. Aminolysis of this compound gave the *cis*-hydroxy amide (**8**), but initially this proved very refractory to reduction with lithium aluminium hydride in tetrahydrofuran (THF). Recalling success in the reduction of some indole-2-carboxamides by replacing THF with *N*-ethylmorpholine,[3] we conducted some probe runs with this solvent, but it was found that the higher reaction temperatures available with this solvent were not the criterion for a successful reaction; the addition of a moderate amount of *N*-ethyl morpholine to the reactants in THF was sufficient to give complete reduction in 2 h at elevated temperature (80 °C), or in 24 h at room temperature. The addition of only 2 equiv. of *N*-ethylmorpholine did not give a marked improvement in the reaction, and so the outcome of the reduction is probably due to the solubilising property of the co-solvent on the intermediate metal hydride/organic substrate complex rather than a metal ligand effect.†



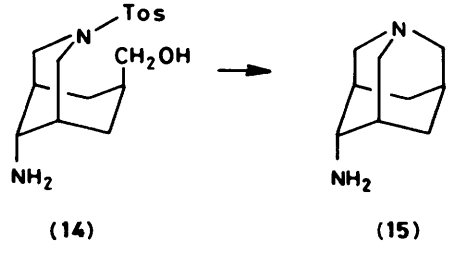
Scheme 1.

Tosylation of the *cis*-amino alcohol (**9**) gave the bis-(*p*-tolylsulphonyl) derivative (**10**), for which the plan was to invert the geometry of the leaving group and thus enable cyclization. However, the latter compound (**10**) failed to react with sodium iodide in boiling acetone, and on applying more forcing conditions [90—95 °C in dimethylformamide (DMF)] a relatively low yield of the benzo-fused tricyclic compound (**12**) was obtained, but no iodo compound (**11**) was detected among the other products.

† Other colleagues have confirmed the beneficial effect of adding *N*-ethylmorpholine as a co-solvent for lithium aluminium hydride reductions of primary and secondary amides of widely differing types. Thus the use of this co-solvent may be a general solution to the problem of a reduction in a state of suspended amination.

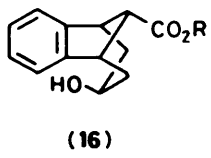


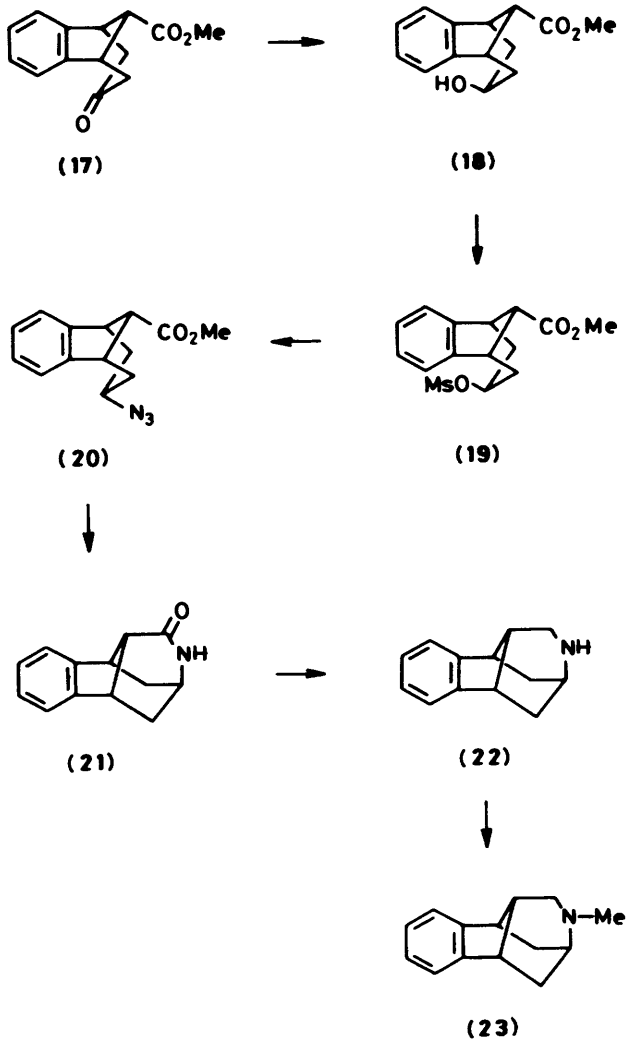
Scheme 2. Tos = *p*-tolylsulphonyl. [a] Numbering scheme for IUPAC-allowed 3,8-ethanoindeno[1,2-*c*]pyrrole ring system name



The reported cyclization of an hydroxy tosylamide (**14**) to an aza-adamantane (**15**) on heating with a mixture of hydrochloric and acetic acids[4] prompted us to try this procedure on compound (**10**). By t.l.c., this procedure appeared to give more of the desired product than did the sodium iodide reaction, but isolation of the material by column chromatography showed it to be a mixture of the desired compound (**12**), and a rearranged product (**13**). Also isolated were two chlorine-containing compounds of molecular formula $C_{20}H_{22}ClNO_2S$, the regio- and stereo-chemistry of which were not investigated.

At this point it seemed that the difficulties of synthesizing the ring system could be overcome if there were an efficient way of obtaining a *trans*-7-hydroxy carboxylic acid derivative (**16**) in high yield. In fact the borohydride reduction of the oxo acid (**3**) does produce the acid (**16**; R = H) in minor amount (*ca.* 17%) but the major product is the lactone (**7**) (69%), most likely because the ionic repulsion between the carboxylate and borohydride anions results in reduction of the keto group from the more sterically hindered side. It was reasoned that reduction of the keto ester (**17**) should allow the expression of this steric





Scheme 3. Ms = methylsulphonyl

hindrance, and this was found to be the case in practice, the *trans*-hydroxy ester (**18**) being obtained in good yield with only minor amounts of *cis*-hydroxy acid and lactone accompanying it. The i.r. spectrum of compound (**18**) has a very pronounced band at 3 597 cm^{-1} for a free hydroxy group. The remaining steps in Scheme 3, mesylation of compound (**18**) to give diester (**19**), substitution of the mesyloxy group with inversion to yield the azido ester (**20**), reduction and cyclization of the latter to give the lactam (**21**), and finally reduction of the amide group to afford the parent compound of this ring system (**22**), were

all straightforward and reasonably high yielding reactions. Perhaps more noteworthy was the Eschweiler–Clark methylation of the secondary amine (**22**) to furnish the tertiary amine (**23**) rapidly, and in high yield, at only 80 °C. In this behaviour, the compound resembles the corresponding secondary amine (**1**; R = H) from the earlier system that was studied.

Experimental

I.r. spectra were recorded with a Perkin-Elmer 681 instrument, and n.m.r. spectra with a Bruker AM 250 spectrometer except for compounds (**13**) and (**14**). M.p.s were determined using a Thomas Hoover capillary m.p. apparatus, and are uncorrected.

7e-(4-*Methoxybenzylamino*)-6,7,8,9-*tetrahydro*-5,9-*methano*-5H-*benzocycloheptene*-10a-*carboxylic acid* (**4**).*—A solution of the oxo acid (**3**) (2.16 g, 10 mmol) and 4-methoxybenzylamine (1.41 g, 10.3 mmol) in methanol (100 cm^3) was treated with sodium cyanoborohydride (2.50 g, 39.7 mmol). The acidity of the reaction mixture was adjusted to pH 6 each morning and afternoon by the addition of a few drops of acetic acid. After the mixture had been stirred at room temperature for 5 days, more sodium cyanoborohydride (630 mg, 10 mmol) was added and after a further 5 days the mixture was acidified carefully with dil. hydrochloric acid (HCN evolution!) and evaporated to dryness. The residue was dissolved in methanol and to the solution was added silica gel (20 g). The suspension was evaporated to dryness and the solid was placed on a column of Merck silica gel 60 (380 g) from which the product (**4**) was isolated by elution with 1:50 ammonium hydroxide–ethanol in a substantially pure state (2.29 g, 71%). The amino acid was recrystallized by evaporation of a solution of the solid in ammonium hydroxide–ethanol in a stream of nitrogen, and was obtained as *needles*, m.p. 185 °C (decomp.) (Found: C, 73.1; H, 7.1; N, 4.1. $C_{21}H_{23}NO_3 \cdot \frac{1}{2}H_2O$ requires C, 72.8; H, 7.0; N, 4.0%); $\nu_{max.}$ 1 636 cm^{-1} (CO_2^-); δ (250 MHz; $CDCl_3$ + a few drops of CF_3CO_2D; Me_4Si) 7.28 (4 H, m, ArH), 7.10 (2 H, d, ArH), 6.85 (2 H, d, ArH), 3.98 (2 H, d, CH_2N), 3.81 (3 H, s, MeO), 3.66 (2 H, m, 5- and 9-H), 3.32 (1 H, t, 10-H), 2.67 (1 H, m, 7-H), and 2.15 (4 H, m, 6- and 8-H_2).

2-(4-*Methoxybenzyl*)-2,3,4,4a,9,9a-*hexahydro*-3,9-*methano*-*indeno*[2,1-c]*pyridin*-1-*one* (**5**).—A mixture of the 4-methoxybenzylamino-acid (**4**) (780 mg, 2.3 mmol), boron trioxide (239 mg, 3.47 mmol), and DMF (4.0 cm^3) was stirred in an oil-bath at 100—105 °C for 20 h. Work-up of the reaction mixture by the addition of water and extraction (ether) gave the *benzotricyclic lactam* (**5**) (425 mg, 58%), m.p. 128.5—129.5 °C (from Pr^i_2O) (Found: C, 79.3; H, 6.7; N, 4.5. $C_{21}H_{21}NO_2$ requires C, 79.0; H, 6.6; N, 4.4%); $\nu_{max.}$(KBr) 1 652 cm^{-1} (CO); δ (250 MHz; $CDCl_3$; Me_4Si) 7.27 (2 H, d, ArH), 7.16 (4 H, m, ArH), 6.87 (2 H, d, ArH), 4.57 (2 H, s, CH_2N), 3.81 (3 H, s, MeO), 3.60 (1 H, m, 3-H), 3.40 (1 H, t, 9a-H), 3.25 (2 H, dd, 4a- and 9-H), 1.79 (2 H, m, 4- and 10-H_{exo}), and 1.58 (2 H, m, 4- and 10-H_{endo}).

2-(4-*Methoxybenzyl*)-2,3,4,4a,9,9a-*hexahydro*-3,9-*methano*-1H-*indeno*[2,1-c]*pyridine* (**6**).—The 4-methoxybenzyl lactam (**5**) (700 mg, 2.2 mmol) was added in portions to a suspension of lithium aluminium hydride (83 mg, 2.2 mmol) in THF (10 cm^3) and the mixture was stirred under reflux under argon for 2 h. After having cooled to 0—5 °C, the reaction mixture was treated with water (0.1 cm^3), followed by 10M-sodium hydroxide (0.05 cm^3), and the mixture was stirred for 0.5 h before filtration. The filtrate was evaporated to afford an oil (663 mg) which was dissolved in dry ether (25 cm^3) and the solution was treated with a slight excess of ethanolic hydrogen chloride to provide the *hydrochloride* of the tertiary amine (**6**) (685 mg, 91%), m.p. 234—236 °C (Found: C, 73.5; H, 7.1; Cl, 10.2; N, 4.1. $C_{21}H_{23}NO \cdot HCl$ requires C, 73.8; H, 7.1; Cl, 10.4; N, 4.1%); δ (250 MHz; $CDCl_3$; Me_4Si) 7.29 (2 H, d, ArH), 7.16 (2 H, m, ArH), 7.08 (2 H, m, ArH), 6.85 (2 H, d, ArH), 3.80 (3 H, s, MeO), 3.67 (2 H, s, CH_2N), 3.06 (2 H, d, 1-H), 3.02 (2 H, dd, 4a- and 9-H), 2.69 (1 H, m, 3-H), 2.44 (1 H, m, 9a-H), 2.29 (2 H, m, 4- and 10-H_{exo}), and 1.48 (2 H, dd, 4- and 10-H_{endo}).

7e-*Hydroxy*-6,7,8,9-*tetrahydro*-5,9-*methano*-5H-*benzocycloheptene*-10a-*carboxamide* (**8**).—The lactone (**7**) (6.51 g, 32.6 mmol) was stirred in a suspension of a mixture of methanol saturated with ammonia (130 cm^3) and ammonium hydroxide (35 cm^3) at ambient temperature for 6 days. Evaporation of the solution yielded the hydroxy amide (**8**) which was slurried with a little water and the mixture was filtered to give the *title compound* (6.31 g, 89%), m.p. 190—192 °C (from hot water) (Found: C, 71.9; H, 7.1; N, 6.4. $C_{13}H_{15}NO_2$ requires C, 71.9; H, 7.0; N, 6.5%); $\nu_{max.}$(KBr) 3 345br (OH) and 1 667 cm^{-1} (CO); δ (250 MHz; CD_3COCD_3; Me_4Si) 7.18 (4 H, m, ArH), 6.84 (1 H, br s, NH), 6.38 (1 H, br s, NH), 3.45 (2 H, m, 7- and 10-H), 3.37 (1 H, d, OH), 2.88 (2 H, m, 5- and 9-H), 1.97 (2 H, m, 6- and 8-H_{exo}), and 1.86 (2 H, m, 6- and 8-H_{endo}).

10a-*Aminomethyl*-6,7,8,9-*tetrahydro*-5,9-*methano*-5H-*benzocyclohepten*-7e-*ol* (**9**).—Lithium aluminium hydride (2.10 g, 55.3 mmol) was added to a mixture of dry THF (50 cm^3) and *N*-ethylmorpholine (20 cm^3) under argon. The hydroxy amide (**8**) (6.00 g, 27.6 mmol) was added in small portions to the stirred mixture, and then the reaction mixture was heated in an oil-bath at 85 °C for 1 h. The mixture was then cooled in an ice-bath during the dropwise addition of water (4.2 cm^3) followed by ammonium chloride (3.0 g). After the mixture had been stirred for 1 h it was filtered, and the filter-cake was stirred with THF (75 cm^3) and the mixture was again filtered. The material isolated from the combined filtrate by evaporation (finally at 0.05 Torr) was purified by column chromatography (180 g of Merck silica gel); the column was eluted first with 1:10:100 ammonium hydroxide–methanol–chloroform to remove the remaining *N*-ethylmorpholine, and then with 1:15:100 solvent mixture to elute the *title product* (3.52 g, 63%), m.p. 148—149 °C (from MeOH–ether) (Found: C, 76.6; H, 8.4; N, 6.8. $C_{13}H_{17}NO$ requires C, 76.8; H, 8.4; N, 6.9%); $\nu_{max.}$(KBr) 3 280br cm^{-1} (OH); δ (250 MHz; $CDCl_3$; Me_4Si) 3.15 (2 H, m, 5- and 9-H), 3.04 (3 H, d, m, CH_2N and 7-H), (1 H, m, 10-H), 1.90 (2 H, m, 6- and 8-H_{exo}), and 1.62 (2 H, m, 6- and 8-H_{endo}).

10a-(p-*Tolylsulphonamidomethyl*)-7e-(p-*tolylsulphonyloxy*)-6,7,8,9-*tetrahydro*-5,9-*methano*-5H-*benzocycloheptene* (**10**).—A mixture of the amino alcohol (**4**) (1.15 g, 5 mmol), toluene-*p*-sulphonyl chloride (2.22 g, 10.7 mmol), and pyridine (10 cm^3) was stirred at room temperature for 72 h. Water was added and the mixture was extracted with ether. The extract was washed three times with 3M-hydrochloric acid, then with saturated sodium chloride, and was then dried over magnesium sulphate before evaporation to dryness. The residual gum crystallized readily from di-isopropyl ether to give the *title compound* (**10**) (2.43 g, 95%), m.p. 155—156 °C (Found: C, 63.6; H, 5.8; N, 2.6; S, 12.5. $C_{27}H_{29}NO_5S_2$ requires C, 63.4; H, 5.7; N, 2.7; S, 12.5); $\nu_{max.}$(KBr) 3 280br (OH), 1 328, and 1 159 cm^{-1} (SO_2); δ(250 MHz; $CDCl_3$; Me_4Si) 7.76 (2 H, d, ArH), 7.56 (2 H, d, ArH), 7.34 (2 H, d, ArH), 7.24 (2 H, d, ArH), 7.15 (2 H, m, ArH), 7.07 (2 H, m, ArH), 7.47 (1 H, t, NH), 3.78 (1 H, m, 7-H), 3.19 (2 H, dd, CH_2N), 3.04 (2 H, m, 5- and 9-H), 3.43 and 3.40 (6 H, 2 s, 2 × Me), 2.17 (1 H, m, 10-H), and 1.82—1.53 (4 H, m, 6- and 8-H_2).

* We have adopted the nomenclature of the previous authors[2] for the bicyclic system and the stereochemical assignments of functional groups.

*Reaction of the Bistoluene-*p*-sulphonyl Derivative* (**10**) *with Sodium Iodide.*—A mixture of the ditosyl derivative (**10**) (512 mg, 1 mmol), sodium iodide (250 mg, 1.67 mmol), and DMF (5 ml) was stirred at 90—95 °C for 72 h. Ether was added and the ethereal solution was washed several times with water, then with saturated sodium chloride, and was dried ($MgSO_4$). The solution was evaporated onto silica gel (3.0 g) and the solid was placed on top of a column of Merck silica gel 60 (75 g). The least polar fraction eluted was the *N*-(p-*tolylsulphonyl*) *benzotricyclic compound* (**12**) (86 mg, 25%), m.p. 206—207 °C (prisms from MeCN) (Found: C, 71.1; H, 6.2; N, 4.2; S, 9.5. $C_{20}H_{21}NO_2S$ requires C, 70.8; H, 6.2; N, 4.1; S, 9.5%); $\nu_{max.}$(KBr) 1 340 and 1 159 cm^{-1} (SO_2); δ (220 MHz; $CDCl_3$; Me_4Si) 7.75 (2 H, d, ArH), 4.00 (1 H, m, 8-H), 3.71 (2 H, m, 1-H), 2.95 (2 H, m, 4a- and 9a-H), 2.74 (1 H, m, 9-H), 2.54 (3 H, s, Me), 2.05 (2 H, m, 4- and 10-H_{exo}), and 1.61 (2 H, m, 4- and 10-H_{endo}).

*Reaction of the Bistoluene-*p*-sulphonyl Derivative* (**10**) *with a Hot Hydrochloric Acid–Acetic Acid Mixture.*—A mixture of the ditosyl derivative (**10**) (2.13 g, 5.98 mmol), acetic acid (53.5 cm^3), and conc. hydrochloric acid (53.5 cm^3) was heated under reflux under argon for 5 h. The reaction mixture was evaporated to dryness, and the residue was shaken with a mixture of methylene dichloride and water. The material isolated from the organic phase was submitted to column chromatography. After a very small early fraction, a solid fraction (768 mg, 38%) was obtained which appeared homogeneous by t.l.c., but the wide m.p. range suggested that the solid was a mixture. Fractional crystallization of the solid from acetonitrile provided the expected product (**12**), m.p. 198—201 °C (no m.p. depression with the product from the iodide reaction).

The more soluble compound (**13**) crystallized in needles, m.p. 137—138 °C (from MeOH) (Found: C, 70.5; H, 6.4; N, 4.1; S, 9.9%; M^+, 339. $C_{20}H_{21}NO_2S$ requires C, 70.8; H, 6.2; N, 4.1; S, 9.5%; *M*, 339); $\nu_{max.}$(KBr) 1 329 and 1 165 cm^{-1} (SO_2); δ (220 MHz; $CDCl_3$; Me_4Si) 7.79 (2 H, d, ArH), 7.27 (2 H, d, ArH), 7.10 (4 H, m, ArH), 4.05 (1 H, t, 3-H), 3.52 (2 H, m, 1-H), 3.18 (2 H, m, 3a- and 8-H), 2.83 (1 H, t, 8a-H), 2.46 (3 H, s, Me), 1.75 (1 H, m, 9-H_{exo}), 1.58 (1 H, m, 10-H_{exo}), 1.33 (1 H, m, 9-H_{endo}), and 0.99 (1 H, m, 10-H_{endo}).

Two more polar compounds were isolated (~80 and 180 mg), and both contained chlorine. Both gave M^+, 375, indicating the molecular formula $C_{20}H_{22}ClNO_2S$.

Methyl 7a-Hydroxy-6,7,8,9-tetrahydro-5,9-methano-5H-benzocycloheptene-10a-carboxylate (**18**).—Sodium borohydride (3.31 g, 87.1 mmol) was added in small portions to a solution of the keto ester (**17**) (10.0 g, 43.5 mmol) in methanol (500 cm^3) at 0—5 °C. By the time hydrogen evolution ceased, reaction was complete, and the mixture was acidified with acetic acid (5.0 cm^3). After evaporation of the mixture to *ca.* 75 cm^3 (carried out <40 °C), water and methylene dichloride were added and the organic extract was washed with water, dried ($MgSO_4$), and evaporated. Purification of the residue by column chromatography (220 g of Merck silica gel 60 eluted with 1:3 ethyl acetate–hexane) yielded the trans-*hydroxy-ester* (**18**) (8.26 g, 82%), m.p. 75—76 °C (from Pr^i_2O) (Found: C, 72.5; H, 7.1. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%); $\nu_{max.}$(KBr) 3 597 (free OH) and 1 728 cm^{-1} (CO); δ (250 MHz; $CDCl_3$; Me_4Si) 7.25 (4 H, m, ArH), 3.82 (1 H, m, 7-H), 3.80 (3 H, s, MeO), 3.42 (2 H, m, 5- and 9-H), 3.28 (1 H, m, 10-H), 2.40 (2 H, m, 6- and 8-H_{exo}), and 1.86 (2 H, d, 6- and 8-H_{endo}).

Methyl 7a-Methylsulphonyloxy-6,7,8,9-tetrahydro-5,9-methano-5H-benzocycloheptene-10a-carboxylate (**19**).—A solution of the *trans*-hydroxy ester (**18**) (6.96 g, 30 mmol) in a mixture of triethylamine (8.3 cm^3, 60 mmol) and dry ether (175 cm^3) was cooled to −78 °C, and was then treated dropwise with a solution of methanesulphonyl chloride (6.87 g, 60 mmol) in dry ether (25 cm^3). The reaction mixture was allowed to attain room temperature; after the mixture had been stirred for 1.5 h, ethyl acetate (400 cm^3) and water (100 cm^3) were added. The organic extract was washed successively with water and saturated aqueous sodium chloride, and dried ($MgSO_4$). Evaporation of the solvent left a solid residue, which was slurried with cold ether and the mixture was filtered to provide pure *mesyl ester* (**19**) (8.24 g, 88%), m.p. 122—123 °C (Found: C, 57.8; H, 5.9; S, 10.4. $C_{15}H_{18}O_5S$ requires C, 58.0; H, 5.9; S, 10.3%); $\nu_{max.}$(KBr) 1 715 (CO), 1 343, and 1 172 cm^{-1} (SO_2); δ (250 MHz; $CDCl_3$; Me_4Si) 7.21 (4 H, m, ArH), 4.94 (1 H, m, 7-H), 3.79 (3 H, s, MeO), 3.41 (2 H, m, 5- and 9-H), 3.30 (1 H, m, 10-H), 2.46 (3 H, s, $MeSO_2$), 2.41 (2 H, m, 6- and 8-H_{exo}), and 2.06 (2 H, d, 6- and 8-H_{endo}).

Methyl 7e-Azido-6,7,8,9-tetrahydro-5,9-methano-5H-benzocycloheptene-10a-carboxylate (**20**).—A mixture of the *trans*-mesyloxy carboxylic ester (**19**) (3.88 g, 12.5 mmol), finely powdered sodium azide (1.22 g, 18.75 mmol), and DMF (78 cm^3) was heated at 80 °C for 1.5 h, then more sodium azide (406 mg, 6.25 mmol) was added and the mixture was heated at 80 °C for a further 1.5 h. Water was added and the crude product was isolated by extraction (ether). Purification of the oil, obtained on work-up, by chromatography (200 g of Merck silica gel 60 eluted with 1:4 ethyl acetate–hexane) gave the *azido ester* (**20**) (2.07 g, 65%) (Found: C, 65.3; H, 6.0; N, 16.2. $C_{14}H_{15}N_3O_2$ requires C, 65.4; H, 5.9; N, 16.3%); $\nu_{max.}$(film) 2 100 (N_3) and 1 735 cm^{-1} (CO); δ (250 MHz; $CDCl_3$; Me_4Si) 7.21 (4 H, m, ArH), 3.80 (3 H, s, MeO), 3.52 (2 H, m, 5- and 9-H), 3.10 (1 H, t, 10-H), 2.71 (1 H, m, 7-H), 1.93 (2 H, m, 6- and 8-H_{exo}), and 1.88 (2 H, dd, 6- and 8-H_{endo}).

2,3,4,4a,9,9a-*Hexahydro-3,9-methanoindeno*[2,1-c]*pyridin-1-one* (**21**).—A mixture of the azido ester (**20**) (1.78 g, 6.94 mmol), methanol (40 cm^3), acetic acid (20 drops), and 5% palladium–charcoal (150 mg) was stirred rapidly in an atmosphere of hydrogen until no starting material remained. The catalyst was filtered off, and the solution, containing two products, was heated under reflux for 24 h to give the lactam (**20**) as the only product (1.58 g). Recrystallization of the solid from acetonitrile furnished the pure *title lactam* (1.32 g, 84%), m.p. 263—265 °C (Found: C, 78.6; H, 6.6; N, 7.0. $C_{13}H_{13}NO$ requires C, 78.4; H, 6.6; N, 7.0%); $\nu_{max.}$(KBr) 1 670 cm^{-1} (CO); δ (250 MHz; $CDCl_3$; Me_4Si) 7.23 and 7.13 (4 H, 2 m, ArH), 3.75 (1 H, quin, 3-H), 3.27 (3 H, m, 4a-, 9-, and 9a-H), 2.03 (2 H, m, 4- and 10-H_{exo}), and 1.75 (2 H, dd, 4- and 10-H_{endo}).

2,3,4,4a,9,9a-*Hexahydro-3,9-methano-1H-indeno*[2,1-c]*pyridine* (**22**).—The lactam (**21**) (846 mg, 4.23 mmol) was added to a suspension of lithium aluminium hydride (400 mg, 10.5 mmol) in THF (32 cm^3) and the mixture was stirred under reflux for 1.5 h. Water (0.3 cm^3) was added dropwise, followed by 5M-sodium hydroxide (1.0 cm^3), and then more water (3.0 cm^3). The solid was filtered off and washed with ether. The combined filtrate was washed successively with water and aqueous sodium chloride, and dried ($MgSO_4$). Evaporation of the solvent afforded the crude base (**22**) (836 mg, ~100%), which was converted into the *hydrochloride* by treatment of an ethereal solution of the secondary amine with ethanolic hydrogen chloride (837 mg, 90%), m.p. 306—309 °C (decomp.) (Found: C, 70.6; H, 7.4; Cl, 16.1; N, 6.3. $C_{13}H_{15}N$·HCl requires: C, 70.4; H, 7.3; Cl, 16.0; N, 6.3%); δ (250 MHz; free base in $CDCl_3$; Me_4Si) 7.15 (4 H, m, ArH), 3.39 (2 H, d, 1-H_2), 3.06 (2 H, dd, 4a- and 9-H), 2.95 (1 H, m, 3-H), 2.40 (1 H, m, 9a-H), 2.12 (2 H, dd, 4- and 10-H_{exo}), and 1.65 (2 H, dd, 4- and 10-H_{endo}).*

* The *endo* protons show a little coupling with 3-H but none to 4a- and 9-H. On the other hand, the *exo* protons are coupled to 4a- and 9-H but not to 3-H.

2-*Methyl*-2,3,4,4a,9,9a-*hexahydro*-3,9-*methano*-1H-*indeno*-[2,1-c]*pyridine* (**23**).—A mixture of the secondary amino hydrochloride (**22**)·HCl (221 mg, 1.0 mmol), sodium formate (68 mg, 1.0 mmol), 37% aqueous formaldehyde (0.09 cm^3), and formic acid (0.15 cm^3) was warmed under a reflux condenser. Reaction began at *ca.* 60—65 °C and was complete in less than 3 h at 80 °C. Basification of the mixture and extraction with ether provided the tertiary amine (**23**) which was converted into the *hydrochloride* (188 mg, 80%), m.p. 278—280 °C (decomp.) (Found: C, 71.0; H, 7.8; Cl, 15.1; N, 5.6. $C_{14}H_{17}N$·HCl requires C, 71.3; H, 7.7; Cl, 15.0; N, 5.9%); δ (250 MHz; free base in $CDCl_3$; Me_4Si) 7.18 (4 H, m, ArH), 3.30 (2 H, m, 1-H), 3.12 (2 H, dd, 4a- and 9-H), 3.01 (1 H, m, 3-H), 2.65 (3 H, s, Me), 2.5 (3 H, m, 4- and 10-H_{endo} and 9a-H), and 1.66 (2 H, d, 4- and 10-H_{exo}).

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