The Synthesis and Stereochemistry of Derivatives of 1,2,3,4,6,11,12,13,14,14a-Decahydropyrido[1,2-*b*][2]benzazonine. Crystal structure of 1,2,3,4,4a,5,6,7,7a,12-decahydro-7-phenylisoindolo[1,2-*d*]quinolizin-13-ium Tosylate

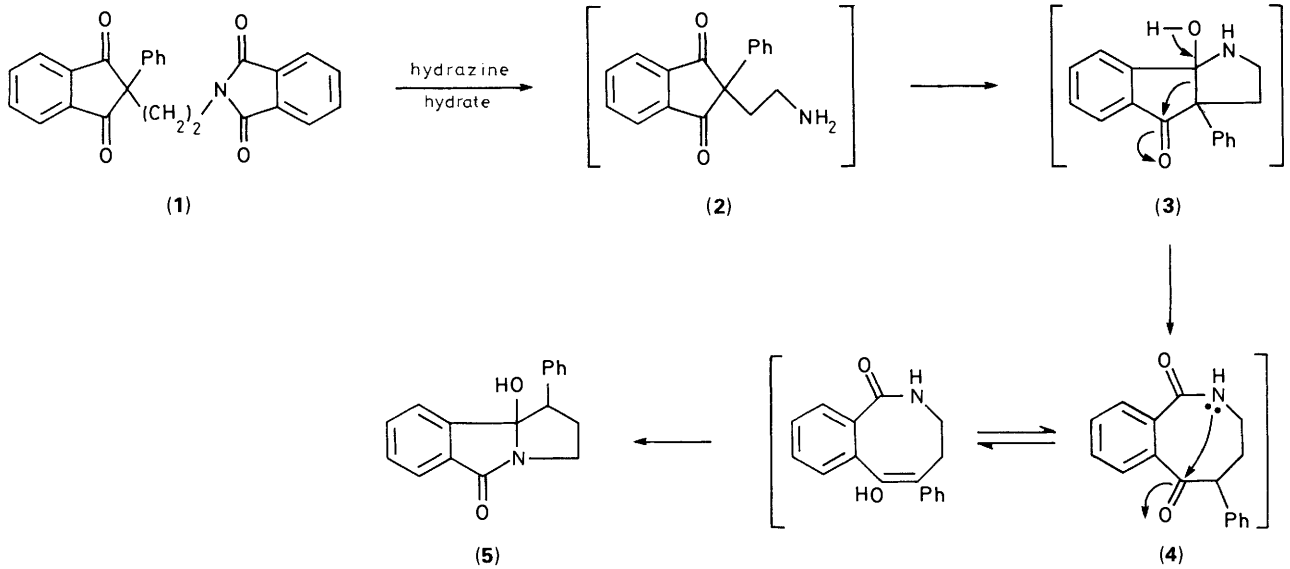
Trevor A. Crabb * **and Craig J. Roxburgh**
Department of Chemistry, Portsmouth Polytechnic, Portsmouth, Hants, PO1 2DT
Roger F. Newton
Glaxo Group Research Limited, Ware, Hertfordshire, SG12 0DJ

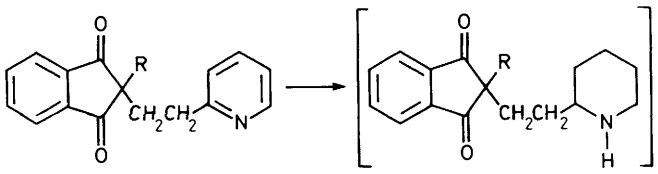
Catalytic reduction of the pyridine ring of 2-phenyl-2-[2-(2-pyridyl)ethyl]indan-1,3-dione gives, by ring opening of the initially produced carbinolamine, 12-phenyl-1,2,3,4,12,13,14,14a- octahydropyrido[1,2-*b*]benzazonine-6,11-dione. This adopts a piperidine ring conformation with an axial alkyl residue, and the low-temperature ^{13}C n.m.r. spectrum shows the presence of two rotamers about the *N*-aroyl moiety. The derived 11-hydroxy-12-phenyldecahydropyrido[1,2-*b*][2]benzazonine prefers the *trans*-fused ring conformation and attempts to form the toluene-*p*-sulphonate of this gave rel-(4a*R*,7*R*,7a*R*,13*R*)-1,2,3,4,4a,5,6,7,7a,12-decahydro-7-phenylisoindolo[1,2-*d*]quinolizin-13-ium tosylate. An *X*-ray structural analysis of the tosylate was performed.

The hydrazinolysis of 2-phenyl-2-(2-phthalimidoethyl)indan-1,3-dione (**1**) gives 1,2,3,9b-tetrahydro-9b-hydroxy-1-phenylpyrrolo[2,1-*a*]isoindol-5-one (**5**) *via* the conversion of 2-(2-aminoethyl)-2-phenylindan-1,3-dione (**2**) into the carbinolamine (**3**) which undergoes ring expansion to 3,4-dihydro-6-hydroxy-5-phenylbenz[3,4]azocin-1(2*H*)-one (**4**) followed by transannular cyclisation to (**5**)[1]. With the synthesis of medium ring heterocycles in mind as possible anxiolytics it was decided to explore the catalytic reduction of the pyridine ring of 2-phenyl-2-[2-(2-pyridyl)ethyl]indan-1,3-dione (**6**) to give the analogue (**9**) of (**2**). The carbinolamine (**12**) derived from this might then be expected to undergo ring expansion to (**15**).

Catalytic reduction of 2-phenyl-2-[2-(2-pyridyl)ethyl]-indan-1,3-dione (**6**), obtained from the Michael addition reaction between 2-phenylindan-1,3-dione and 2-vinylpyridine in boiling ethanol, over Adams platinum oxide catalyst in methanol in the presence of hydrochloric acid afforded a single isomer of 12-phenyl-1,2,3,4,12,13,14,14a-octahydropyrido[1,2-*b*][2]benzazonine-6,11-dione (**15**) as a white crystalline solid, m.p. 222 °C. The i.r. spectrum of this exhibited only one band in the region 1 700—1 750 cm^{-1} at 1 705 cm^{-1} indicating the absence of the indanedione moiety [*cf.* 1 740 and 1 705 cm^{-1} in (**6**)] and the band at 1 640 cm^{-1} suggested the presence of the tertiary amide group.

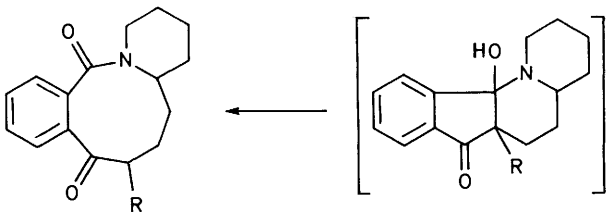
The signal broadening in the ^1H n.m.r. spectrum of (**15**) recorded at 25 °C indicated the presence of the two benzoyl rotamers at near coalescence temperature. The spectrum recorded at −20 °C in CD_2Cl_2 showed clear signals for the predominant rotamer (>96%) (**15a**). In particular the 4-methylene protons absorbed at δ 4.4 and 2.6 characteristic of rotamer (**15a**). The ^{13}C n.m.r. spectrum of (**15**) in CD_2Cl_2 at −26 °C showed signals for both rotamers [*ca.* 96% (**15a**), 4% (**15b**)].





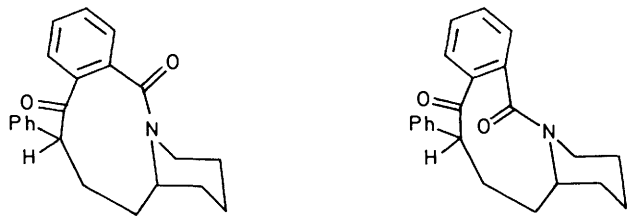
(6) R = Ph
(7) R = p-$MeOC_6H_4$
(8) R = p-ClC_6H_4

(9) R = Ph
(10) R = p-$MeOC_6H_4$
(11) R = p-ClC_6H_4



(15) R = Ph
(16) R = p-$MeOC_6H_4$
(17) R = p-ClC_6H_4

(12) R = Ph
(13) R = p-$MeOC_6H_4$
(14) R = p-ClC_6H_4

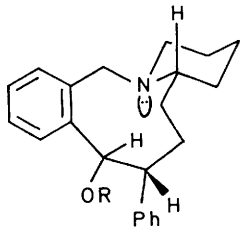


(15a) (15b)

Since it has been shown[2] that 2-alkyl-*N*-benzoylpiperidines adopt chair conformations with axial alkyl groups, (**15**) is expected to adopt the analogous conformations (**15a**) and (**15b**).

This is confirmed by the ^{13}C n.m.r. chemical shifts of the piperidine ring nuclei which resemble those for *N*-benzoyl-2-methylpiperidine[3] possessing an axial methyl group. Characteristic of such a *cis*-fusion is the highfield shift of C-2 (δ 19) as a consequence of the γ-axial interaction with C-14. Dreiding models of (**15a**) indicate a pseudo-equatorial orientation of the phenyl group. In such a structure the dihedral angles between the 12-H and 13-H bonds are *ca.* 90° and *ca.* 150° which, from the Karplus relationship, give couplings of 0 and 9 Hz in good agreement with the observed absorption for 12-H (δ 4.22) ($J_{12,13}$ 0, 9.9 Hz).

In connection with the ring enlargement (**12**) ⟶ (**15**) it was decided to synthesize and study the catalytic reduction of 2-*p*-methoxyphenyl-2-[2-(2-pyridyl)ethyl]indan-1,3-dione (**7**) since the electron-donating properties of the *p*-methoxyphenyl group in the derived carbinolamine (**13**) may affect this reaction. The synthesis was achieved by treatment of the phthalide, prepared by the reduction of phthalic anhydride with sodium borohydride in dimethylformamide,[4] with anisaldehyde to yield 2-*p*-methoxyphenylindan-1,3-dione[5] in excellent yield. This readily added 2-vinylpyridine to yield (**7**). Hydrogenation of the pyridine ring of (**7**) over Adams platinum oxide catalyst at atmospheric pressure and room temperature gave 2-*p*-methoxyphenyl-2-[2-(2-piperidyl)ethyl]-indan-1,3-dione (**13**) rather than (**16**).



(18) R = H
(19) R = Ac
(20) R = Bz

This failure of the reaction (**13**) to (**16**) suggested that an electron-withdrawing group in the position *para* to the 2-aryl substituent in 2-aryl-2-[2-(2-piperidyl)ethyl]indan-1,3-dione may aid ring expansion and for this reason 2-*p*-chlorophenyl-2-[2-(2-pyridyl)ethyl]indan-1,3-dione (**8**) was chosen for synthesis.

2-*p*-Chlorophenylindan-1,3-dione[6] would not undergo a Michael addition with 2-vinylpyridine in boiling ethanol but addition was finally achieved by refluxing 2-*p*-chlorophenylindan-1,3-dione and 2- vinylpyridine under aprotic conditions for 48 h in benzene solvent using Triton B as a catalyst. Catalytic hydrogenation of the resulting 2-*p*-chlorophenyl-2-[2-(2-pyridyl)ethyl]indan-1,3-dione (**8**) in hydrochloric acid and ethanol solvent, gave 12-*p*-chlorophenyl-1,2,3,4,12,13,-14,14a-octahydropyrido[1,2-*b*][2]benzazonine-6,11-dione (**17**), the spectra and stereochemistry of which were essentially identical with those of 12-phenyl-1,2,3,4,12,13,14,14a-octahydropyrido[1,2-*b*][2]benzazonine-6,11-dione (**15**). Lithium aluminium hydride reduction of (**15**) gave 12-phenyl-1,2,3,4-12,13,14,14a-octahydropyrido[1,2-*b*][2] benzazonin-11-ol (**18**), the ^1H n.m.r. spectrum of which shows the signals for the C-6 protons at δ 3.3 and 4.5 (J_{gem} − 15.2 Hz).

This large chemical-shift difference between the methylene protons adjacent to nitrogen is typical of *trans*-fusion between the piperidine and benzazonine rings.[7] The broad doublet at δ 4.7 (*J* 12 Hz) was reduced to a broad singlet after the addition of D_2O and was therefore assigned to 11-H. Since $J_{11\text{-H},12\text{-H}}$ is *ca.* 0 Hz the dihedral angle between the 11-H and 12-H bonds has to be *ca.* 90° and examination of Dreiding models gives the relative orientation of the 11- and 12-substituents as shown in (**18**). Decoupling of the signal at δ 4.7 sharpens the broadened doublet at δ 3.3 permitting assignment of the signals at δ 3.3 to the C-12 proton. Analysis of these signals shows $J_{12\text{-H},13\text{-H}'}$ 10 Hz, $J_{12\text{-H},13\text{-H}''}$ 0 Hz indicating that the dihedral angle between it and one of the C-13 protons is *ca.* 90°. Decoupling of the broad doublet at δ 3.3 (J_{gem} −13 Hz) simplified the signals in the region δ 2.2 indicating that these signals are due to 4-H_{eq} and 4-H_{ax} respectively. The large difference in chemical shifts between the C-4 methylene protons of 1.1 p.p.m. indicates a *trans*-fusion between the piperidine ring and the nine-membered ring. Comparison of the ^{13}C n.m.r. shifts of the piperidine nuclei with those in other *trans*-fused heterocycles[8] confirm the *trans*-fusion.

The spectra of the derived acetate (**19**) and benzoate (**20**) are also in accord with the *trans*-fused conformation. The spectrum of the toluene-*p*-sulphonate of (**18**) however showed marked differences to those of (**19**) and (**20**) with lowfield signals for protons adjacent to nitrogen, indicating formation of *rel* (4a*R*,7*S*,7a*R*,13*S*)-1,2,3,4,4a,5,6,7,7a,12-decahydro-7-phenyl-isoindolo[1,2-*d*]quinolizin-13-ium tosylate (**21**). The ^1H n.m.r. spectrum of the tosylate showed a doublet at δ 5.8 ($J_{7a,7}$ 7 Hz) assigned to 7a-H and decoupling of this located 7-H at δ 4.7. The C-12 protons absorbed as an AB quartet at (δ 4.7, δ 4.5, *J*

Table. Atom co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses

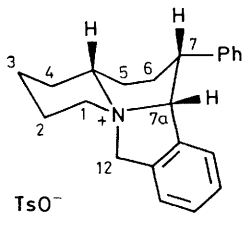
Atom	*x*	*y*	*z*
N(1)	8 522(1)	−2.784(2)	1 711(1)
C(2)	8 909(1)	−1 347(2)	1 761(1)
C(3)	9 140(1)	−1 182(2)	2 569(1)
C(4)	9 662(2)	−179(3)	2 897(2)
C(5)	9 804(2)	−212(3)	3 659(2)
C(6)	9 452(2)	−1 222(3)	4 080(1)
C(7)	8 929(1)	−2 229(2)	3 753(1)
C(8)	8 773(1)	−2 191(2)	2 989(1)
C(9)	8 243(1)	−3 166(2)	2 507(1)
C(10)	7 261(1)	−3 069(2)	2 573(1)
C(11)	6 925(1)	−1 782(2)	2 178(1)
C(12)	7 057(2)	−1 884(3)	1 342(1)
C(13)	7 773(1)	−2 863(2)	1 142(1)
C(14)	8 087(2)	−2 645(3)	362(1)
C(15)	8 756(2)	−3 699(3)	164(1)
C(16)	9 505(2)	−3 647(3)	722(1)
C(17)	9 206(1)	−3 812(2)	1 510(1)
C(18)	7 039(1)	−3 226(2)	3 379(1)
C(19)	6 770(2)	−2 145(2)	3 808(1)
C(20)	6 599(2)	−2 325(3)	4 549(1)
C(21)	6 694(2)	−3 581(3)	4 878(1)
C(22)	6 965(2)	−4 687(3)	4 458(1)
C(23)	7 133(1)	−4 510(2)	3 717(1)
O(24)	5 735(1)	−4 906(2)	896(1)
O(1)	7 253(1)	3 764(2)	1 374(1)
O(2)	7 935(1)	1 576(2)	1 448(1)
O(3)	8 332(1)	3 363(2)	2 333(1)
S(1)	7 669(1)	2 760(1)	1 856(1)
C(25)	6 878(1)	2 178(2)	2 465(1)
C(26)	6 036(1)	2 011(2)	2 202(1)
C(27)	5 418(1)	1 607(2)	2 681(1)
C(28)	5 616(2)	1 365(2)	3 423(1)
C(29)	6 457(2)	1 523(2)	3 678(1)
C(30)	7 088(1)	1 920(2)	3 200(1)
C(31)	4 927(2)	943(4)	3 949(2)
O(32)	4 312(1)	3 500(2)	466(1)

[a] *X*-Ray data have been deposited at the Cambridge Crystallographic Data Centre.* [b] The numbering of the atoms in the *X*-ray structural formula corresponds to that in the Table. This is however, different from the conventional numbering system used in the text.

* For details of the deposition scheme see 'Instructions for Authors (1989),' *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue 1.

−15.2 Hz). Decoupling of the broad doublet at δ 3.2 (J_{vic} 13 Hz) simplified the group of signals at δ 4.7 permitting assignments of the signals at δ 4.7 and 3.2 to 1ax-H and 1eq-H respectively.

The ^{13}C n.m.r. spectrum of the tosylate is in accord with structure (**21**). In particular the highfield absorption (δ 18.1) of C-2 is consistent with the axial C-12 methylene group.



(**21**)

The stereochemistry of the tosylate (**21**) was determined on the basis of *X*-ray crystallographic results (see Table and Figure) and this enabled the relative configurations at C-12 and C-14a in (**15**) and of C-11, C-12, and C-14a in (**18**) to be deduced.

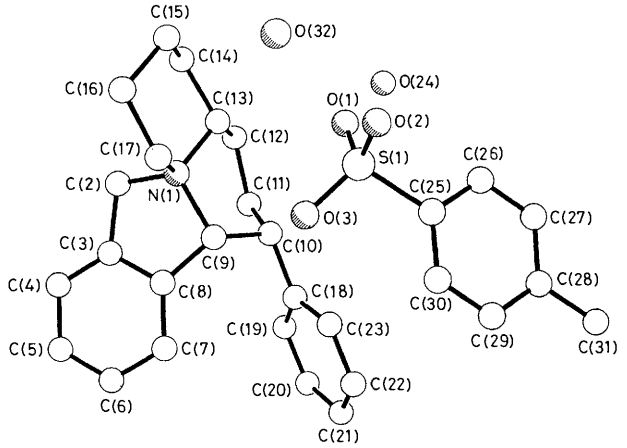


Figure. *X*-Ray crystal structure of (**21**)

Experimental

Elemental analyses were carried out at Glaxo Group Research Limited. U.v. spectra were recorded on a Shimadzu 240 spectrometer in solutions of absolute ethanol. ^1H N.m.r. and ^{13}C n.m.r. spectra were determined on a JEOL GSX spectrometer at 270 and 68 MHz. Mass spectra were recorded on a JEOL JMS-DX303 mass spectrometer. The m.p.s were determined in sealed tubes and are uncorrected.

Crystal Data.—$C_{29}H_{37}NO_5S$, M = 511.7, monoclinic, a = 15.581(4), b = 9.731(2), c = 17.987(7) Å, β = 92.33(3)°, U = 2 725 Å^3, space group $P2_1/a$, Z = 4, D_c = 1.25 g cm^{-3}, Cu radiation, λ = 1.541 78 Å, μ(Cu-K_α) = 13 cm^{-1}, F(000) = 1 096. Data were measured on a Nicolet R3m diffractometer with Cu-K_α radiation (graphite monochromator) using ω-scans. 3 681 Independent reflections were measured (20 ⩽ 116°), of which 3 328 had $|F_o| > 3\sigma(|F_o|)$ and were considered to be observed. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied. The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. A ΔF map revealed the presence of two water molecules. The leading proton on the methyl group on the sp^2 centre was also located from a ΔF map. The protons on the water molecules were located from a ΔF map and refined isotropically. The positions of the remaining hydrogen atoms were idealised, C–H = 0.96 Å, assigned isotropic thermal parameters, U(H) = 1.2 U_{eq}(C), and allowed to ride on their parent carbon atoms. The methyl group was refined as a rigid body. Refinement was by block-cascade, full-matrix least-squares to R = 0.040, R_w = 0.048 [$w^{-1} = \sigma^2(F) + 0.000\,42F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.20 and −0.21 e Å^{-3} respectively. The mean and maximum shift/error in the final refinement were 0.037 and 0.198 respectively. Computations were carried out on an Eclipse S140 computer using the SHELXTL program system.

2-Phenyl-2-[2-(2-pyridyl)ethyl]indan-1,3-dione (**6**).—2-Vinylpyridine (10 g) was added to a solution of 2-phenylindan-1,3-dione (25 g) in ethanol (100 ml) and the reaction mixture heated under reflux for 20 h. The solid which crystallised out on cooling was filtered off and recrystallised from methanol to give the title compound as pale yellow crystals (30 g, 97%), m.p. 72 °C; $\nu_{max.}$(CHCl$_3$) 1 740, 1 710, and 1 600 cm^{-1}; $\lambda_{max.}$(EtOH) 210 infl., 227, and 250 infl. nm; δ_H(CDCl$_3$) 8.4 (1 H, s, ArH), 6.9—8.1 (12 H, m, ArH), and 2.74 (4 H, s, CH_2CH_2) (Found: C, 80.5; H, 5.1; N, 4.3. $C_{22}H_{17}NO_2$ requires C, 80.7; H, 5.2; N, 4.3%).

12-*Phenyl*-1,2,3,4,12,13,14,14a-*octahydropyrido*[1,2-*b*]-[2]-*benzazonine*-6,11-*dione* (**15**).—The dione (**6**) (16.4 g), Adams platinum oxide catalyst (1 g), and concentrated hydrochloric acid (10 ml) were stirred in methanol (300 ml) under hydrogen at atmospheric pressure, until absorption of hydrogen ceased. The catalyst was then filtered off and the filtrate evaporated under reduced pressure. The resultant concentrate was basified with aqueous sodium carbonate and extracted with ether and the ether extract dried (Na_2SO_4). Evaporation of the ether gave a white gum, which was purified by column chromatography over Woelm neutral alumina (grade III) to afford the title compound (**15**) as white needles (10 g, 60%), m.p. 222 °C; $\nu_{max.}$(Nujol) 1 705 and 1 640 cm^{-1}; $\lambda_{max.}$(EtOH) 217 nm; $\delta_H((CD_3)_2SO$ 7.0—7.7 (9 H, m, ArH), 4.4 (d, *J* 9.9 Hz, 12-H), 4.2 (1 H, d, 4eq-H), 3.75 (1 H, m, 14a-H), 2.65 (1 H, td, 4ax-H), 2.25 (1 H, m, 13-H), and 1.2—2.0 (9 H, m, aliphatic); $\delta_C(CD_2Cl_2$, −20 °C), Rotamer (**15a**): C-1 30.7, C-2 19.4, C-3 25.4, C-4 37.8, C-6 169.7, C-11 210.1, C-12 57.6, C-13 34.5, C-14 28.5, and C-14a 54.1; Rotamer (**15b**): C-1 30.7, C-2 19.4, C-3 24.2, C-4 43.6, C-6 172.9, C-11 203.2, C-12 53.4, C-13 31.7, C-14 26.7, and C-14a 51.1 (Found: C, 79.3; H, 71; N, 4.1. $C_{22}H_{23}NO_2$ requires C, 79.3; H, 7.0; N, 4.2%).

12-*Phenyl*-1,2,3,4,12,13,14,14a-*decahydropyrido*[1,2-b][2]-*benzazonin*-11-*ol* (**18**).—The dione (**15**) (1 g, 3 mmol) in tetrahydrofuran (25 ml) was added to a stirred slurry of lithium aluminium hydride (1 g) in tetrahydrofuran (100 ml) and the resulting mixture was warmed for 20 h. After this period water was carefully added and the mixture filtered and extracted with chloroform. The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a colourless oil. This oil was taken up in light petroleum (b.p. 40—60 °C) and left until the title compound crystallised as prisms (0.75 g, 78%), m.p. 98—99 °C; $\nu_{max.}$(Nujol) 3 500, 1 600, and 750 cm^{-1}; $\lambda_{max.}$(EtOH) 210 (ε 20 500) and 260nm (ε 900); $\delta_H(CDCl_3)$ (1 H, br d, OH), 7.1—7.3 (9 H, m, ArH), 4.7 (1 H, 11-H), 4.5 (1 H, 6-H), 3.3 (2 H, 12-H and 6-H), 3.3 (1 H, br d, 4eq-H), 2.2 (1 H, m, 4ax-H), 2.4 (1 H, m, 14a-H), and 1.3—2.9 (10 H, m, aliphatic); $\delta_C(CDCl_3)$ C-1 33.0, C-2 25.1, C-3 26.4, C-4 53.6, C-6 59.4, C-11 81.6, C-12 53.6, C-13 30.2, C-14 23.8, and C-14a 60.0 (Found: C, 82.2; H, 8.6; N, 4.3. $C_{22}H_{27}NO$ requires C, 82.2; H, 8.4; N, 4.3%).

12-*Phenyl*-1,2,3,4,6,11,12,13,14,14a-*decahydropyrido*[1,2-b]-[2]*benzazonin*-11-*yl Acetate*.—The alcohol (**18**) (0.3 g, 0.93 mmol) was added to acetyl chloride (3 ml) and the mixture left overnight at room temperature. The mixture was then poured into ice-cold saturated aqueous sodium hydrogen carbonate and the solid that formed filtered off and washed with water. It was then dissolved in warm dilute hydrochloric acid and the solution basified with aqueous sodium hydrogen carbonate to give a solid. This was washed with water and dried *in vacuo* to give the title compound as a white powder (0.32 g, 94%), m.p. 57—61 °C; $\nu_{max.}$(Nujol) 1 730, 1 600, and 750 cm^{-1}; $\lambda_{max.}$(EtOH) 210 (ε 20 000) and 255 (1 000); $\delta_H(CDCl_3)$ 6.4—7.4 (9 H, m, ArH), 6.95 (1 H, d, 11-H), 3.2, 4.2 (2 H, AB, 6-H), 3.4 (1 H, bd, 4eq-H), 3.25 (1 H, dd, 12-H), 2.61 (1 H, m, 4ax-H), 2.4 (1 H, m, 14a-H), 2.0 (3 H, s, CH_3), and 1.2—2.6 (10 H, m, aliphatic); $\delta_C(CDCl_3)$ C-1 32.6, C-2 24.7, C-3 26.8, C-4 54.3, C-6 56.4, C-11 71.9, C-12 47.4, C-13 30.0, C-14 22.1, and C-14a 61.8 (Found: C, 79.4; H, 8.0; N, 3.9. $C_{24}H_{29}NO_2$ requires C, 79.3; H, 8.0; N, 3.85%).

12-*Phenyl*-1,2,3,4,12,13,14,14a-*decahydropyrido*[1,2-b][2]-*benzazonin*-11-*yl Benzoate*.—Benzoyl chloride (1 g) was added to an ice cooled solution of the alcohol (**18**) (0.5 g, 1.6 mmol) in dry pyridine (5 ml) and the mixture left at 0 °C overnight. The red mixture was then poured into saturated aqueous sodium hydrogen carbonate (100 ml) containing ice and the mixture extracted with chloroform. The combined extracts were dried (Na_2SO_4) and evaporated to leave a dark oil. Chromatography of this using ether–light petroleum (80:20) as the eluant gave a colourless oil (0.38 g, 57%) which crystallised with time. One crystallisation from light petroleum (b.p. 40—60 °C) gave the title compound as a white crystalline solid, m.p. 134—135 °C; $\nu_{max.}$(liquid film) 1 710 and 1 600 cm^{-1}; $\lambda_{max.}$(EtOH) 205 (ε 73 000), 225infl. and 270 (1 531); *m/z* 425 (M^+); $\delta_H(CDCl_3)$ 7.0 (1 H, 11-H), 4.3, 3.2 (2 H, AB, 6-H), 3.4 (1 H, br d, 4eq-H), 3.4 (1 H, dd, 12-H), 2.6 (1 H, m, 4ax-H), and 2.4 (1 H, m, 14a-H); $\delta_C(CDCl_3)$ C-1 33.4, C-2 25.4, C-3 27.5, C-4 55.1, C-6 57.2, C-11 73.1, C-12 48.0, C-13 30.8, C-14 22.6, and C-14a 62.5 (Found: C, 81.8; H, 7.3; N, 3.3. $C_{29}H_{31}NO_2$ requires C, 81.9; H, 7.3; N, 3.3%).

1,2,3,4,4a,5,6,7,7a,12-*Decahydro*-7-*phenylisoindolo*[1,2-d]-*quinolizin*-13-*ium Tosylate* (**21**).—The alcohol (**18**) (1 g, 3.1 mmol) was dissolved in dry pyridine (1 ml) and the solution cooled to 0 °C. Freshly crystallized toluene-*p*-sulphonyl chloride (0.635 g) in pyridine (0.55 ml) was then added and the mixture left at 0 °C overnight. After this it was poured onto crushed ice–water (100 ml) and saturated aqueous sodium hydrogen carbonate added to give a colourless crystalline precipitated. This was filtered off, washed with water, and dried *in vacuo* to yield the title compound (**21**) (0.95 g, 64%), m.p. 120—125 °C. A sample of the tosylate for the *X*-ray structural analysis was recrystallised from ethanol; $\nu_{max.}$(Nujol) 1 600, 1 410, 1 160, and 750 cm^{-1}; $\lambda_{max.}$(EtOH) 210 (ε 21 000) and 260 (650); $\delta_H(CDCl_3)$ 7.9, 7.2 (4 H, m, TsH), 6.9 (8 H, m, ArH), 5.8 (1 H, d, 7a-H), 5.6 (1 H, d, ArH), 4.7 (1 H, dt, 1ax-H), 4.7, 4.5 (2 H, AB, *J* 15.2 Hz, 12-H), 4.7 (1 H, 7-H), 4.47 (1 H, m, 7a-H), 3.25 (1 H, br d, 1eq-H), 2.3 (3 H, s, TsMe), and 1.5—2.2 (10 H, m, aliphatic); $\delta_C(CDCl_3)$ C-1 57.2, C-2 18.1, C-3 26.3, C-4 28.7, C-4a 61.4, C-5 21.2, C-6 21.2, C-7 38.8, C-7a 84.3, and C-12 63.25 (Found: C, 73.6; H, 7.0; N, 3.0. $C_{29}H_{33}NO_3S$ requires C, 73.3; H, 6.9; N, 2.9%).

2-p-*Methoxyphenylindan*-1,3-*dione*.—This compound was prepared by the method of Shapiro.[5] Phthalide (8 g, 75 mmol) was dissolved in methanol (100 ml) and sodium (4.2 g) added with cooling, the temperature being maintained < 5 °C. *p*-Methoxybenzaldehyde (8.16 g, 75 mmol) was then added followed by ethyl acetate (16 g). The mixture was heated at 65 °C for 75 min on a steam-bath during which time the reaction mixture turned red. The solvents were removed under reduced pressure and to the remaining residue water (200 ml) was added. Acidification of the aqueous layer with 6M hydrochloric acid (35 ml) gave a solid which was filtered off and recrystallised from absolute ethanol to give the title compound as long needles (12.4 g, 83%), m.p. 152—154 °C (lit.,[5] 154—155.5 °C); $\nu_{max.}$(Nujol) 1 540, 1 700, and 1 600 cm^{-1}; $\delta_H(CDCl_3)$ 7.8—8.2 [4 H, m, $(CO)_2ArH$], 6.8—7.2 (4 H, m, MeO*ArH*), and 3.8 (4 H, s, CH_2CH_2).

2-p-*Chlorophenylindan*-1,3-*dione*.—This compound was prepared by the method of Lombardino and Wiseman.[6] Into dried methanol (250 ml) was added sodium (3.5 g). phthalide (20 g, 149 mmol), and *p*-chlorobenzaldehyde (20.37 g, 149 mmol), Dried ethyl acetate (38 ml) was then added and the resulting mixture heated on a steam-bath at 65 °C for 2 h during which time the mixture turned deep red. All the solvents were removed under reduced pressure to give a thick red oil. Water (100 ml) was added to this and the mixture extracted with ether. The aqueous layer was acidified with concentrated hydrochloride and the resulting mixture extracted with chloroform. The chloroform extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a thick red oil. Column chromatography over silica using diethyl ether–ethyl acetate (50:50) as the eluant gave a white crystalline solid, recrystallisation of which from absolute ethanol gave the title compound as

colourless needles (10.8 g, 28%), m.p. 143—144 °C (lit.,[6] 145—145.5 °C); $\nu_{max.}$(Nujol) 3 400, 1 735, and 1 600 cm^{-1}; $\delta_H(CDCl_3)$ 7.6—8.0 [4 H, m, $(CO)_2ArH$], 6.8—7.3 (4 H, m, ClArH), and 4.2 (1 H, s, ClPhCH).

2-p-*Methoxyphenyl*-2-[2-(2-*pyridyl*)*ethyl*]*indan*-1,3-*dione* (**7**).—2-*p*-Methoxyphenylindan-1,3-dione (5 g, 20 mmol) was dissolved in benzene (50 ml) and Triton B (50 mg) followed by 2-vinylpyridine (2.5 g) were added. The mixture was heated under reflux for 30 h after which it was evaporated to give a thick oil. Chromatography of this over silica using ethyl acetate–light petroleum (b.p. 60—80 °C) gave the title compound (**7**) as a colourless oil (3.9 g, 84%); $\nu_{max.}$(liquid film) 1 740, 1 700, 1 600, and 750 cm^{-1}; $\lambda_{max.}$(EtOH) 226 (ε 6 000), 250 (9 000), 260infl, 265infl., and 270 infl.; $\delta_H(CDCl_3)$ 6.8—8.5 (12 H, ArH), 3.7 (3 H, s, OMe), and 2.6—2.8 (4 H, m, CH_2CH_2); *m/z* 357 (M^+) (Found: C, 76.4; H, 5.5; N, 3.9. $C_{18}H_{19}N$ requires C, 77.3; H, 5.4; N, 3.9%).

2-p-*Chlorophenyl*-2-[2-(2-*pyridyl*)*ethyl*]*indan*-1,3-*dione* (**8**).—The dione (**7**) (4 g) was added to benzene (250 ml) together with 2-vinylpyridine (1.75 g) and Triton B (30 mg) and the mixture refluxed for 40 h. The mixture was then evaporated under reduced pressure to give a thick oil which, taken up in a little absolute alcohol and left, provided a white crystalline solid. This recrystallised from absolute alcohol to give 2-*p*-chlorophenyl-2-[2-(2-pyridyl)ethyl]indan-1,3-dione as a white crystalline solid (4.7 g, 84%), m.p. 176—177 °C; $\nu_{max.}$(Nujol) 1 740, 1 700, 1 600, and 750 cm^{-1}; $\delta_H(CDCl_3)$ 6.8—8.4 (12 H, ArH), and 2.6 (4 H, s, CH_2CH_2) (Found: C, 73.05; H, 4.4; N, 3.9. $C_{22}H_{16}NO_2Cl$ requires C, 73.0; H, 4.4; N, 3.9%).

2-p-*Methoxyphenyl*-2-[2-(2-*piperidyl*)*ethyl*]*indan*-1,3-*dione* (**10**).—The dione (**7**) (8.3 g) was dissolved in methanol (200 ml) and concentrated hydrochloric acid (3 ml) followed by PtO_2 (0.6 g) were added. The mixture was hydrogenated at atmospheric pressure and room temperature until the calculated amount of hydrogen had been taken up. The catalyst was filtered off and the solvent removed under reduced pressure. Saturated sodium hydrogen carbonate was then added and the mixture extracted with chloroform. The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a black oil. Chromatography of this over silica gave the title compound as a colourless oil; $\nu_{max.}$(liquid film) 3 400, 1 740, 1 700, 1 600, and 750 cm^{-1}; $\delta_H(CDCl_3)$ 6.8—7.8 (8 H, m, ArH), 3.8 (3 H, s, OMe), 4.9 (1 H, s, NH), and 1.0—3.5 (13 H, m, aliphatic). Heating resulted in decomposition and this precluded microanalysis.

12-p-*Chlorophenyl*-1,2,3,4,12,13,14,14a-*octahydropyrido*-[1,2-b][2]*benzazonine*-6,11-*dione* (**17**).—The dione (**8**) (10.5 g, 29 mmol) was dissolved in methanol (200 ml) and concentrated hydrochloric acid (4 ml). PtO_2 (1 g) was added and the mixture hydrogenated at atmospheric pressure and room temperature until the calculated amount of hydrogen had been taken up. The catalyst was filtered off and the solvent removed under reduced pressure. Saturated aqueous sodium hydrogen carbonate was added and the mixture extracted with chloroform. The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure. Heating to 78 °C for 15 min gave a white crystalline solid, recrystallisation of which from absolute ethanol gave the *title compound* as a white crystalline solid, m.p. 212—214 °C; $\nu_{max.}$(Nujol) 1 740, 1 700, 1 600, and 750 cm^{-1}; $\lambda_{max.}$(EtOH) 218 (ε 15 500) and 230 infl.; $\delta_H[(CD_3)_2SO]$ 7.3—7.7 (8 H, m, ArH), 4.5 [d, C(Ph)–H], 4.2 (1 H, m, NCH_{eq}), 3.8 [1 H, m, $C(Ph)CH_2CH_2C$-H_{ax}], 2.65 (1 H, t, N-CH_{ax}), 2.25 [1 H, m, $C(Ph)CH_{eq}$], and 1.2—2.2 (9 H, m, aliphatic); *m/z* 369 and 368 (M^+) (Found: C, 71.9; H, 6.1; N, 3.7. $C_{22}H_{22}ClNO_2$ requires C, 71.8; H, 6.0; N, 3.8%).

References

1 T. A. Crabb, A. Patel, R. F. Newton, and T. J. Cholerton, *J. Chem. Soc., Perkin Trans. 1*, 1985, 191.
2 R. A. Johnson, *J. Org. Chem.*, 1968, **33**, 3627.
3 E. Wenkert, J. S. Bindra, C-J. Chang, D. W. Cochran, and T. M. Schell, *Acc. Chem. Res.*, 1974, **7**, 46.
4 D. M. Bailey and R. E. Johnson, *J. Org. Chem.*, 1970, **35**, 3574.
5 S. L. Shapiro, K. Geiger, J. Youleu, and C. Freedman, *J. Org. Chem.*, 1961, **26**, 3580.
6 J. G. Lombardino and E. H. Wiseman, *J. Med. Chem.*, 1968, **11**, 342.
7 T. A. Crabb and A. R. Katritzky, *Adv. Heterocycl. Chem.*, 1984, **36**, 1.
8 L. Banting, T. A. Crabb, and A. N. Trethewey, *Magn. Reson. Chem.*, 1987, **25**, 352.

Received 10*th May* 1989; *Paper* 9/01962F