Some Isoindolo-fused Heterocyclic Systems by Cyclodehydration of *N*-Arylalkyl-3-hydroxyphthalimidines

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α-Hydroxy lactams formed by reduction or Grignard addition to appropriately *N*-substituted phthalimides (**1a**—**d**) undergo acid-catalysed cyclodehydration to derivatives of the isoindolo-fused heterocyclic systems (**6**)—(**10**). Ring closures to the naphthalene 2- or 8-position are observed to occur with *N*-1-naphthylalkyl substituents, the latter proved by an *X*-ray crystal structure determination of 13b-phenyl-7*H*-benz[*de*]isoindolo[1,2-*a*]isoquinolin-9(13*H*)-one (**9b**).

Intramolecular amidoalkylation *via* the acid-catalysed cyclisation of α-hydroxy lactams is a useful approach to the construction of fused heterocyclic systems,[1] with important applications in alkaloid synthesis.[2,3] In particular, this method has been employed previously with *N*-substituted hydroxyphthalimidines (**2c, f, g, k**) to obtain fused isoindoles (**4**), (**5a, b**), and (**7a**), respectively.[4,5] In related reactions, the isoindolo[2,1-*f*]phenanthridines (**8a, b**) were obtained by acid treatment of 3-aminophthalide derivatives (**3a, b**),[6] and the fused heterocycles (**6a**), (**7b**), and (**8b**) in single-step procedures from *o*-acylbenzoic acids and the appropriate amines.[5,6] Our aim has been to extend the scope of this general procedure to the synthesis of new heterocyclic systems,[7] and we report here the results obtained with a series of α-hydroxy lactams (**2a, b, d, e, h**—**j**). These include the use of trifluoroacetic acid for the cyclisation step and the formation of new fused heterocycles (**9**) and (**10**) from *N*-1-naphthylalkyl substituted intermediates.

Results and Discussion

The α-hydroxy lactams (**2d, h, i**) were obtained by reduction of the corresponding phthalimides (**1b**—**d**) using sodium borohydride in the presence of acid, the method developed by Speckamp and co-workers,[8,9] but modified by the use of toluene-*p*-sulphonic acid. For reduction of (**1e**) it was necessary to omit the acid in order to avoid some concomitant reduction of the *N*-allyl group. As the use of sodium borohydride with *N*-aryl imides not uncommonly leads to ring-opened by-products,[9,10] a preferable method for *N*-biphenyl-2-ylphthalimide (**1a**) was photochemical reduction in propan-2-ol.[11] Other α-hydroxy lactams (**2b, e, j**) were the products of Grignard addition to the phthalimides (**1a, b, d**). These results are summarised in Table 1.

The tryptamine derivative (**2i**) cyclised spontaneously under the weakly acidic conditions used for work-up of the borohydride reaction and gave the known isoindolo[1,2-*a*]-β-carboline (**6a**).[5] Compound (**2a**) was heated in trichloroacetic acid and afforded the known isoindolo[2,1-*f*]phenanthridine (**8a**).[6] Cyclodehydration of the other hydroxyphthalimidines was accomplished in refluxing trifluoroacetic acid to give the new isoindolo-fused heterocyclic products detailed in Table 1. The use of trifluoroacetic acid is cleaner, work-up is simpler, and yields are generally better than those achieved in similar cyclisations in hot polyphosphoric acid.

There is a noteworthy difference between the patterns of cyclisation shown by the 1-naphthylmethyl compounds (**2d, e**) and by the homologous 2-(1-naphthylethyl) lactam (**2h**). The structure (**10**) of the cyclisation product from (**2h**) is based on analogy with that of the known 13-azasteroid (**12**), which is formed by acid treatment of a mixture of the α-hydroxy lactam (**11a**) and its ethyl ether (**11b**).[12] This is supported by the ^{1}H n.m.r. spectrum of (**10**) recorded at 300 MHz which shows a pattern for the naphthyl hydrogens very like that recorded for 1,2-dimethylnaphthalene[13] and significantly different from the more symmetrical pattern observed for 1,8-dimethylnaphthalene. However, cyclisation of compounds (**2d, e**) involved attack at the naphthalene 8-position instead, to give (**9a, b**), respectively. The ^{1}H n.m.r. absorptions for the naphthyl hydrogens of (**9a**) clearly resemble those for 1,8-dimethylnaphthalene,[13] and the correctness of structure (**9b**) was established by *X*-ray crystallography (Figure). The results of n.m.r. decoupling experiments also confirm a 1,8-disubstituted naphthalene structure for the related compound (**13**).[10]

Interestingly, formation of a 6-membered ring is preferred in both cases. Application of Baldwin's rules[14] to the ring closure of an *N*-acyliminium ion intermediate shows that the alternative cyclisation of (**2d, e**) to the naphthalene 2-position would be a disfavoured 5-*endo-trigonal* process with respect to the C=N bond, leading to the formation of structure (**14**). However, in the case of (**2h**) the choice is between 6- or 7-*endo-trigonal* ring closure to the naphthalene 2- or 8-position, respectively. Although similar cyclisations to form a 7-membered ring in (**7a, b**) have been reported,[5] our result demonstrates the preference for formation of a 6-membered ring.

The *N*-allyl-α-hydroxy lactams (**2l, m**) failed to cyclise on treatment with acid. This accords with other cases reported,[15] in which ring closure of an *N*-acyliminium ion intermediate (**15**) would require a disfavoured 5-*endo-endo-trigonal* process.

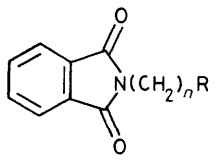
Table 1. α-Hydroxy lactam and fused heterocyclic products

Phthalimide	Reducing Agent	Hydroxy-lactam	Yield (%)	Cyclised product	Yield (%)
(**1a**)	$Pr^iOH/h\nu$	(**2a**)	68	(**8a**)	26
	$PhCH_2MgCl$	(**2b**)	78	(**8c**)	99
(**1b**)	$NaBH_4$	(**2d**)	97	(**9a**)	46
	PhMgBr	(**2e**)	62	(**9b**)	77
(**1c**)	$NaBH_4$	(**2h**)	23[a]	(**10**)	70
(**1d**)	$NaBH_4$	(**2i**)	[b]	(**6a**)	69
	PhMgBr	(**2j**)	100	(**6b**)	42
(**1e**)	$NaBH_4$	(**2l**)	85	—	0
	PhMgBr	(**2m**)	35	—	0

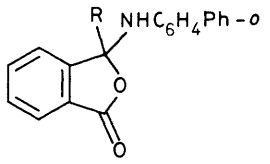
[a] And (**1c**) recovered (76%). [b] Product (**6a**) isolated after acidic work-up.

Experimental

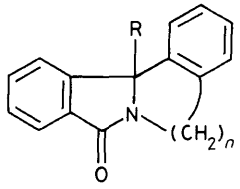
I.r. spectra were recorded for Nujol mulls and calibrated with polystyrene (Pye-Unicam 1025 and SP3-200 and Perkin-Elmer 257 and 1420 spectrophotometers). ^{1}H N.m.r. spectra were



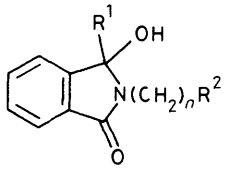
(1) **a**; n = 0, R = o-PhC_6H_4
b; n = 1, R = α-$C_{10}H_7$
c; n = 2, R = α-$C_{10}H_7$
d; n = 2, R = indol-3-yl
e; n = 1, R = $CH{=}CH_2$



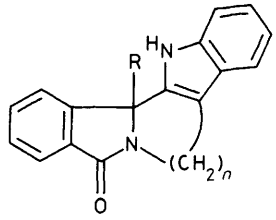
(3) **a**; R = H
b; R = Ph



(4) n = 1, R = Ph
(5) **a**; n = 2, R = H
b; n = 2, R = Ph



(2) **a**; n = 0, R^1 = H, R^2 = o-PhC_6H_4
b; n = 0, R^1 = $PhCH_2$, R^2 = o-PhC_6H_4
c; n = 1, R^1 = R^2 = Ph
d; n = 1, R^1 = H, R^2 = α-$C_{10}H_7$
e; n = 1, R^1 = Ph, R^2 = α-$C_{10}H_7$
f; n = 2, R^1 = H, R^2 = Ph
g; n = 2, R^1 = R^2 = Ph
h; n = 2, R^1 = H, R^2 = α-$C_{10}H_7$
i; n = 2, R^1 = H, R^2 = indol-3-yl
j; n = 2, R^1 = Ph, R^2 = indol-3-yl
k; n = 3, R^1 = H, R^2 = indol-3-yl
l; n = 1, R^1 = H, R^2 = $CH{=}CH_2$
m; n = 1, R^1 = Ph, R^2 = $CH{=}CH_2$



(6) **a**; n = 2, R = H
b; n = 2, R = Ph
(7) **a**; n = 3, R = H
b; n = 3, R = Ph

recorded at 60 (Varian EM360-A), 90 (JEOL-JNM-FX90Q), or 300 MHz (Bruker MSL300) for solutions in [^{2}H]chloroform (unless otherwise stated) with tetramethylsilane as internal standard. Mass spectra were obtained by electron impact at 70 eV (Kratos MS30). Preparative t.l.c. was performed on silica-coated plates using centrifugal assistance to achieve radial separation (Chromatotron), whereby all new compounds were obtained chromatographically pure. Light petroleum refers to the fraction b.p. 40—60 °C. Ether and tetrahydrofuran for Grignard reactions were dried before use.

Phthalimides (**1a**—**e**).—The phthalimides (**1a**, **c**, **d**) were prepared from phthalic anhydride and the corresponding amines; their m.p. in agreement with reported values.[16—18]

Sodium hydride (0.21 g) was added to phthalimide (1.0 g) in *N*,*N*-dimethylformamide (10 ml) at 0 °C. The solution was allowed to warm to room temperature and stored for 2.5 h before addition of 1-(chloromethyl)naphthalene (1.2 g) in *N*,*N*-dimethylformamide (10 ml). The mixture was stirred for 24 h and then poured into water and extracted with chloroform. The extract was washed repeatedly with water, dried ($MgSO_4$), and evaporated to dryness. The residue on recrystallisation from ethanol gave *N*-(1-naphthylmethyl)phthalimide (**1b**) (1.4 g, 72%), m.p. 178.5—180.5 °C (lit.,[16] 179—180 °C).

N-Allylphthalimide (**1e**) was prepared *via* a Mitsunobu reaction[19] from phthalimide (0.2 g), allyl alcohol (0.09 g), and triphenylphosphine (0.36 g) in tetrahydrofuran (10 ml), to which was added diethyl azodicarboxylate (0.236 g) in tetrahydrofuran (4 ml). This mixture was stirred for 17 h and then evaporated to dryness. Chromatography of the residue using chloroform as eluant gave *N*-allylphthalimide (**1e**) (0.17 g, 68%), m.p. 69—71 °C (lit.,[20] 69—70 °C).

Reduction of Phthalimides (**1a**—**e**).—*N*-Biphenyl-2-ylphthalimide (**1a**) (0.2 g) in propan-2-ol (100 ml) was irradiated for 48 h with a Hanovia 125 W medium-pressure mercury arc lamp in a water-cooled quartz apparatus with nitrogen bubbling through the solution. The solution was boiled with addition of activated charcoal (2 g) and then filtered, and the solvent removed by rotary evaporation. The crude product was purified by preparative t.l.c. and the hydroxy lactam (**2a**) (138 mg, 68%) eluted with ethyl acetate–chloroform (1:10, v/v), m.p. 178—180 °C (from toluene–light petroleum) (lit.,[21] m.p. 169—171 °C), with i.r., ^{1}H n.m.r., and mass spectra in agreement with those reported.[21]

To *N*-(1-naphthylmethyl)phthalimide (**1b**) (0.26 g) in ethanol (100 mol) at 0 °C was added sodium borohydride (0.24 g) and toluene-*p*-sulphonic acid (2M solution in ethanol; 0.6 ml). The mixture was stirred with continuous addition of further toluene-*p*-sulphonic acid (2M solution in ethanol; 0.6 ml h^{-1}). After 7 h the mixture was poured into saturated aqueous sodium hydrogen carbonate and extracted with chloroform. The chloroform extract was washed with dilute hydrochloric acid and aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated under reduced pressure. The product was purified by preparative t.l.c. with ether as eluant, to afford the *α-hydroxy lactam* (**2d**)

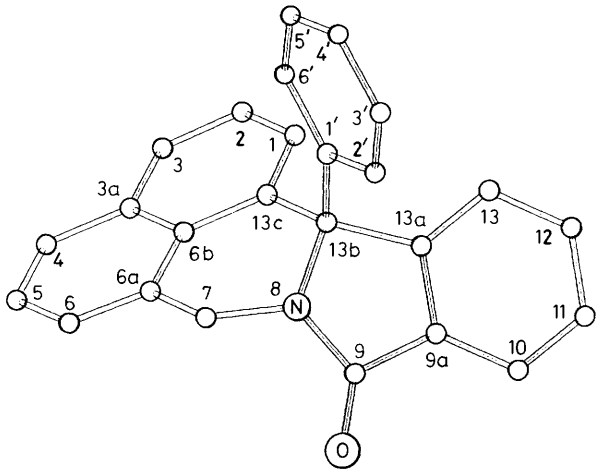
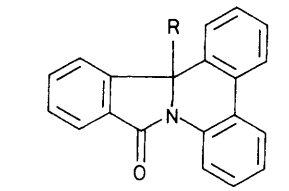
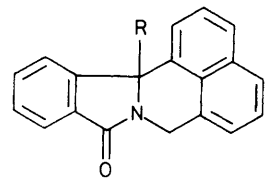


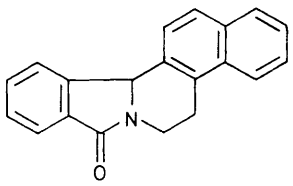
Figure. The molecular structure and numbering of compound (**9b**) (hydrogen atoms omitted).



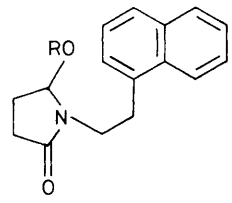
(**8**) **a**; R = H
b; R = Ph
c; R = $PhCH_2$



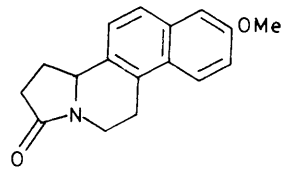
(**9**) **a**; R = H
b; R = Ph



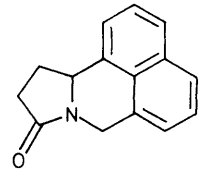
(**10**)



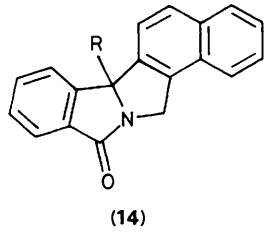
(**11**) **a**; R = H
b; R = Et



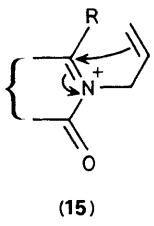
(**12**)



(**13**)



(**14**)



(**15**)

(253 mg, 97%), m.p. 195—198 °C (from ethanol) (Found: M^+, 289.1104. $C_{19}H_{15}NO_2$ requires M^+, 289.1103; $\nu_{max.}$ 3 305 (OH) and 1 675 cm^{-1} (CO); δ_H 4.80 and 5.49 (each 1 H, d, J 15.5 Hz, CH_2), 5.59 and 6.78 (each 1 H, d, J 10.5 Hz, 3-H and OH, respectively), and 7.45—8.45 (11 H, m, ArH); m/z 289 (M^+, 23%), 156 (100), 141 (32), 129 (18), and 105 (22).

N-[2-(1-Naphthylethyl)]phthalimide (**1c**) (0.18 g) was dissolved in methanol (80 ml) at 0 °C and sodium borohydride (0.15 g) was added over 20 min. The mixture was stirred for 4 h and then poured into aqueous sodium hydrogen carbonate and worked up as before. Preparative t.l.c. using ethyl acetate–chloroform (1:4, v/v) gave unchanged phthalimide (**1c**) (136 mg, 76%) followed by the *α-hydroxy lactam* (**2h**) (42 mg, 23%), m.p. 186—187 °C (from toluene–light petroleum) (Found: M^+, 303.1259. $C_{20}H_{17}NO_2$ requires M^+, 303.1259); $\nu_{max.}$ 3 290br (OH) and 1 665 cm^{-1} (CO); δ_H 3.25—4.10 (4 H, m, CH_2CH_2), 5.88 and 6.74 (each 1 H, d, J 8.1 Hz, 3-H and OH, respectively), 7.10—8.05 (10 H, m), and 8.20—8.40 (1 H, m, ArH); m/z 303 (M^+, 77%), 211 (20), 210 (17), 162 (45), 154 (70), 141 (22), 133 (100), 115 (22), 105 (20), and 77 (20).

N-[2-(Indol-3-yl)ethyl]phthalimide (**1d**) (0.20 g) in ethanol (50 ml) at −10 °C was reduced with sodium borohydride (0.15 g) with gradual addition of toluene-*p*-sulphonic acid (2M solution in ethanol; 0.6 ml h^{-1}) over 6 h. More toluene-*p*-sulphonic acid was added to bring pH < 2, and the mixture was stirred for 48 h at room temperature and then poured into saturated aqueous sodium hydrogen carbonate and extracted with chloroform. The extract was washed, dried, and evaporated, as before. Preparative t.l.c. with ethyl acetate–chloroform (1:4, v/v) as eluant afforded 8,13b-dihydro-isoindolo[1,2-*a*]-β-carbolin-5(7*H*)-one (**6a**) (131 mg, 69%), m.p. 206—209 °C (from ethanol) (lit.,[5] m.p. 210—214 °C) (Found: C, 78.5; H, 5.3; N, 10.2%; M^+ − H, 273.1025. Calc. for $C_{18}H_{13}N_2O$: C, 78.8; H, 5.1; N, 10.2%; M^+ − H, 273.1028).

Sodium borohydride (0.20 g) in methanol (20 ml) was added over 20 min to a stirred solution of *N*-allylphthalimide (**1e**) (0.20 g) in methanol (80 ml) at 0 °C. The mixture was stirred for 3 h and then poured into saturated aqueous sodium hydrogen carbonate and extracted with chloroform. The extract was washed, dried ($MgSO_4$), and evaporated under reduced pressure to leave a yellow oil. The product was separated by preparative t.l.c. using chloroform as eluant to give *2-allyl-2,3-dihydro-3-hydroxy-isoindol-1-one* (**2l**) (172 mg, 85%), m.p. 92—93.5 °C (from toluene—light petroleum) (Found: M^+, 189.0792. $C_{11}H_{11}NO_2$ requires M^+, 189.0790); $\nu_{max.}$ 3 285br (OH) and 1 680 cm^{-1} (CO); δ_H 3.73 (1 H, dd, J 16.2 and 6.3 Hz, NC*H*H'), 4.14 (1 H, m, NCH*H'*), 5.00—5.20 (2 H, m) and 5.64—6.01 (2 H, m, CH=CH_2 and 3-H), and 7.28—7.65 (4 H, m, ArH); m/z 189 (M^+, 75%), 172 (13), 160 (12), 134 (25), 133 (100), 125 (23), 105 (63), and 77 (14).

Grignard Additions to Phthalimides (**1a**—**e**).—The Grignard reagent (1.2 mmol) was prepared from benzyl chloride (0.15 g) and magnesium (0.03 g) in ether (5 ml). This solution was cooled to −70 °C before addition of *N*-biphenyl-2-yl-phthalimide (**1a**) (0.20 g) in tetrahydrofuran (5 ml). The mixture was stirred at −70 °C for 2.5 h and then allowed to warm to room temperature when it was poured into saturated aqueous ammonium chloride and extracted with chloroform. The extract was washed, dried ($MgSO_4$), and evaporated under reduced pressure. The residual solid was purified by preparative t.l.c. using chloroform as eluant to afford *3-benzyl-2-biphenyl-2-yl-2,3-dihydro-3-hydroxy-isoindol-1-one* (**2b**) (177 mg, 78%), m.p. 196—198 °C (from ethanol) (Found: $M^+ - H_2O$, 373.1471. $C_{27}H_{19}NO^+$ requires 373.1467); $\nu_{max.}$ 3 210br (OH) and 1 670 cm^{-1} (CO); m/z M^+, absent, 374 (25%), 373 ($M^+ - H_2O$, 100), 300 (28), and 282 (27). ^1H and ^{13}C N.m.r. spectra complicated by extra lines showing the presence of two conformational isomers (*ca.* 3:2 ratio) due to restricted rotation of the *N*-biphenylyl substituent: δ_C 43.8 and 44.9 (both t, CH_2); δ_H (major isomer) 1.16 (1 H, d, J 2 Hz, OH), 2.68 (1 H, dd, J 13.7 and 2 Hz C*H*H), 3.37 (1 H, d, J 13.7 Hz, CH*H*), 6.42 and 7.87 (each 1 H, d, J 7 Hz, ArH), and

6.85—7.70 (16 H, m, other ArH); (minor isomer) 1.63(br) and 2.97 (each 1 H, d, *J* 13.8 Hz, CH_2), 3.70 (1 H, s br, OH), 6.26 (1 H, d, *J* 7.5 ArH), and 6.85—7.70 (17 H, m, other ArH).

The phthalimide (**1b**) (0.20 g) in tetrahydrofuran (8 ml) was added to a solution of the Grignard reagent (1.4 mmol) freshly prepared from bromobenzene (0.22 g) and magnesium (34 mg) in ether (5 ml). This solution was stirred for 20 h at room temperature and then worked up as before. Preparative t.l.c. with chloroform as eluant afforded 2,3-*dihydro*-3-*hydroxy*-2-(1-*naphthylmethyl*)-3-*phenylisoindol*-1-*one* (**2e**) (160 mg, 62%), m.p. 128—129 °C (from toluene–light petroleum) (Found: M^+, 365.1410. $C_{25}H_{19}NO_2$ requires M^+, 365.1416); $\nu_{max.}$ 3 295br (OH), and 1 690 cm^{-1} (CO); δ_H 3.94 (1 H, s, OH), 4.60 and 5.19 (each 1 H, d, *J* 15.4 Hz, CH_2), 6.75—7.85 (15 H, m, ArH), and 8.13 (1 H, m, ArH); *m/z* 365 (M^+, 6%), 210 (22), 181 (19), 158 (14), 156 (100), 141 (20), and 115 (14).

The Grignard reagent (2.8 mmol) was prepared from bromobenzene (0.44 g) and magnesium (0.07 g) in ether (5 ml). This solution was cooled to −20 °C before addition of the phthalimide (**1d**) (0.20 g) in tetrahydrofuran (10 ml). The mixture was stirred for 4 h at −20 °C and then worked up as before. Preparative t.l.c. with ether as eluant afforded 2,3-*dihydro*-3-*hydroxy*-2-[2-(*indol*-3-*yl*)*ethyl*]-3-*phenylisoindol*-1-*one* (**2j**) (0.29 g, 100%), m.p. 310.5—311.5 °C (from toluene–light petroleum) (Found: M^+, 368.1522. $C_{24}H_{20}N_2O_2$ requires M^+, 368.1525); $\nu_{max.}$ 3 210br (OH) and 1 670 cm^{-2} (CO); δ_H[$(CD_3)_2SO$] 2.70—3.20 (4 H, m, CH_2CH_2), 4.40 (1 H, s br, OH), 6.83—8.10 (14 H, m, ArH), and 11.45 (1 H, s, NH); *m/z* 368 (M^+, 15%), 350 (24), 273 (49), 209 (32), 143 (100), and 130 (35).

The Grignard reagent (5.3 mmol) was prepared from bromobenzene (0.84 g) and magnesium (0.13 g) in ether (5 ml). This solution was cooled to 0 °C before addition of the phthalimide (**1e**) (0.2 g) in tetrahydrofuran (8 ml). The mixture was stirred for 5 h at 0 °C and then worked up as before. Preparative t.l.c. with chloroform as eluant afforded 2-*allyl*-2,3-*dihydro*-3-*hydroxy*-3-*phenylisoindol*-1-*one* (**2m**) (99 mg, 35%), m.p. 143—144 °C (from toluene–light petroleum) (Found: M^+, 265.1106. $C_{17}H_{15}NO_2$ requires M^+, 265.1103); $\nu_{max.}$ 3 250 (OH) and 1 695 cm^{-1} (CO); δ_H 3.52 and 3.93 (each 1 H, dd, *J* 15.6 and 6.2 Hz, NCH_2), 4.75—5.70 (3 H, m, $CH{=}CH_2$), 5.15 (1 H, s br, OH), and 7.05—7.62 (9 H, m, ArH); *m/z* 265 (M^+, 23%), 210 (52), 209 (100), 188 (M − Ph, 26), 181 (16), 153 (14), 152 (27), 130 (21), 105 (21), 104 (20) 77 (23), and 56 (40).

Fused Heterocyclic Products.—The hydroxy lactam (**2a**) (0.10 g) and trichloroacetic acid (5.0 g) were heated together for 4 h at 100 °C after which the mixture was cooled and added to an excess of saturated aqueous sodium hydrogen carbonate. The mixture was extracted with chloroform and the extract dried ($MgSO_4$), and evaporated under reduced pressure. Purification by preparative t.l.c. using chloroform as eluant afforded isoindolo[2,1-*f*]-phenanthridin-10(14bH)-one (**8a**) (25 mg, 26%), 178—181 °C (from toluene–light petroleum) (lit.,[6] m.p. 178—181 °C); i.r., ^1H n.m.r., and mass spectra in agreement with those reported.[6]

The general procedure used for the other hydroxy lactams involved heating under reflux in trifluoroacetic acid (4 ml) for the time stated, then neutralisation of the acid, and work-up as described above for reaction in trichloroacetic acid. The hydroxy lactam (**2b**) (50 mg) heated for 4 h in trifluoroacetic acid; preparative t.l.c. using chloroform as eluant gave 14b-*benzyl-isoindolo*[2,1-f]*phenanthridin*-10(14bH)-*one* (**8c**) (47 mg, 99%), m.p. 196—197 °C (from toluene–light petroleum) (Found: M^+, 373.1464. $C_{27}H_{19}NO$ requires M^+, 373.1467); $\nu_{max.}$ 1 690 cm^{-1} (CO); δ_H 3.17 and 3.25 (each 1 H, d, *J* 13.7 Hz, CH_2) and 6.42—6.60 (2 H, m), 6.86—7.16 (3 H, m), and 7.18—8.22 (12 H, m, ArH); *m/z* 373 (M^+, 1%), 283 (23), 282 (M − $PhCH_2$, 100), 254 (10), and 253 (3).

The hydroxy lactam (**2d**) (124 mg) heated for 7 h in trifluoroacetic acid; preparative t.l.c. using ethyl acetate–chloroform (1:6, v/v) as eluant afforded 7H-*benz*[de]*isoindolo*[1,2-a]*isoquinolin*-9-(13bH)-*one* (**9a**) (53 mg, 46%), recrystallised from ethanol, (decomp.) > 170 °C (Found: M^+ − H, 270.0915. $C_{19}H_{12}NO$ requires 270.0919); $\nu_{max.}$ 1 685 cm^{-1} (CO); δ_H 4.72 and 4.79 (each 1 H, d, *J* 16.7 Hz, CH_2), 5.89 (1 H, s, 13b-H), and 7.26—8.15 (10 H, m, ArH); *m/z* 271 (M^+, 88%), 270 (100), 240 (20), 135 (11), and 120 (22).

The hydroxy lactam (**2e**) (55 mg) heated for 2.5 h in trifluoroacetic acid; preparative t.l.c. using chloroform as eluant afforded the 13b-*phenyl derivative* (**9b**) (40 mg, 77%), m.p. 258—259 °C (from ethanol) (Found: M^+, 347.1311. $C_{25}H_{17}NO$ requires M^+, 347.1310); $\nu_{max.}$ 1 695 cm^{-1} (CO); δ_H 4.34 and 5.71 (each 1 H, d, *J* 17.2 Hz, CH_2), and 6.68—8.09 (15 H, m, ArH); *m/z* 347 (M^+, 43%), 271 (20), 270 (M − Ph, 100), and 240 (19).

The hydroxy lactam (**2h**) (29 mg) heated for 6 h in trifluoroacetic acid; preparative t.l.c. using ethyl acetate–chloroform (1:4, v/v) as eluant afforded 5,6-*dihydrobenz*[f]*isoindolo*-[1,2-a]*isoquinolin*-8(12bH)-*one* (**10**) (20 mg, 70%), m.p. 185—186 °C (decomp.) (from toluene–light petroleum) (Found: M^+, 285.1129. $C_{20}H_{15}NO$ requires M^+, 285.1153; $\nu_{max.}$ 1 675 cm^{-1} (CO); δ_H 3.24 (2 H, m, CH_2Ar), 3.40 and 4.80 (each 1 H, m, CH_2N), 5.80 (1 H, s, 12b-H), and 7.24—7.93 (10 H, m, ArH); *m/z* (M^+, 68%), 284 (M − H, 77), 256 (24), 92 (38), and 91 (55).

The hydroxy lactam (**2j**) (81 mg) heated for 3.5 h in trifluoroacetic acid; preparative t.l.c. using chloroform as eluant afforded 8,13b-*dihydro*-13b-*phenylisoindolo*[1,2-a]-β-*carbolin*-5-(7H)-*one* (**6b**) (32 mg, 42%), m.p. 298—300 °C (decomp.) (from toluene–light petroleum) (Found: M^+, 350.1414. $C_{24}H_{18}N_2O$ requires M^+, 350.1419); $\nu_{max.}$ 3 210br (NH) and 1 660 cm^{-1} (CO); δ_H 2.49—4.18 (4 H, m, CH_2), 6.72—7.69 (13 H, m, ArH), and 8.06 (1 H, s br, NH); *m/z* 350 (M^+, 42%), 274 (22), and 273 (M − Ph, 100).

The hydroxy lactams (**2l, m**) were recovered unchanged after

Table 2. Fractional atomic co-ordinates for compound (**9b**)[a,b]

Atom	*x/a*	*y/b*	*z/c*
C(1)	−0.318 2(2)	0.342 0(3)	−0.086 6(3)
C(2)	−0.348 1(2)	0.181 2(3)	−0.015 7(4)
C(3)	−0.326 4(2)	0.104 2(3)	−0.110 5(4)
C(3a)	−0.271 6(2)	0.184 8(3)	−0.278 8(3)
C(4)	−0.245 3(3)	0.108 1(3)	−0.376 5(4)
C(5)	−0.190 5(3)	0.188 3(4)	−0.536 3(4)
C(6)	−0.160 9(3)	0.348 5(3)	−0.606 7(4)
C(6a)	−0.185 4(2)	0.428 1(3)	−0.519 0(3)
C(6b)	−0.241 4(2)	0.347 9(3)	−0.350 2(3)
C(7)	−0.153 9(3)	0.599 7(3)	−0.596 4(4)
N(8)	−0.226 2(2)	0.643 7(2)	−0.528 2(2)
C(9)	−0.304 8(2)	0.690 6(3)	−0.631 1(3)
O	−0.314 3(2)	0.726 1(3)	−0.797 5(2)
C(9a)	−0.371 2(2)	0.694 9(3)	−0.499 8(3)
C(10)	−0.457 3(2)	0.744 8(3)	−0.532 1(4)
C(11)	−0.501 7(2)	0.744 8(4)	−0.383 4(5)
C(12)	−0.460 5(2)	0.698 7(3)	−0.208 5(4)
C(13)	−0.374 3(2)	0.649 1(3)	−0.176 5(4)
C(13a)	−0.332 6(2)	0.644 2(3)	−0.324 5(3)
C(13b)	−0.236 9(2)	0.600 4(3)	−0.330 0(3)
C(13c)	−0.267 8(2)	0.424 8(3)	−0.251 7(3)
C(1′)	−0.128 7(2)	0.700 6(3)	−0.242 7(3)
C(2′)	−0.089 4(2)	0.859 9(3)	−0.307 7(4)
C(3′)	0.005 4(3)	0.956 2(3)	−0.230 7(4)
C(4′)	0.063 1(2)	0.894 8(3)	−0.087 5(4)
C(5′)	0.025 3(3)	0.737 4(4)	−0.023 0(4)
C(6′)	−0.069 1(2)	0.640 0(3)	−0.099 4(4)

[a] Numbering as in the Figure. [b] Estimated standard deviations ($\times 10^4$) are given in parenthesis.

Table 3. Bond lengths (Å) for non-hydrogen atoms in (**9b**)[a,b]

C(1)–C(2)	1.402(4)	C(11)–C(12)	1.375(4)
C(2)–C(3)	1.358(4)	C(12)–C(13)	1.388(4)
C(3)–C(3a)	1.408(4)	C(9a)–C(13a)	1.373(3)
C(3a)–C(4)	1.408(4)	C(13)–C(13a)	1.375(3)
C(4)–C(5)	1.354(4)	N(8)–C(13b)	1.460(3)
C(5)–C(6)	1.397(4)	C(13a)–C(13b)	1.523(3)
C(6)–C(6a)	1.360(3)	C(1)–C(13c)	1.366(3)
C(3a)–C(6b)	1.422(3)	C(6b)–C(13c)	1.415(3)
C(6a)–C(6b)	1.418(3)	C(13b)–C(13c)	1.535(3)
C(6a)–C(7)	1.499(3)	C(13b)–C(1′)	1.534(3)
C(7)–N(8)	1.444(3)	C(1′)–C(2′)	1.373(3)
N(8)–C(9)	1.354(3)	C(2′)–C(3′)	1.381(4)
C(9)–O	1.214(3)	C(3′)–C(4′)	1.363(4)
C(9)–C(9a)	1.473(4)	C(4′)–C(5′)	1.358(4)
C(9a)–C(10)	1.390(4)	C(5′)–C(6′)	1.381(4)
C(10)–C(11)	1.377(4)	C(6′)–C(1′)	1.375(3)

[a] Numbering as in the Figure. [b] Estimated standard deviations ($\times 10^3$) are given in parenthesis.

heating under reflux in formic acid. Decomposition of (**2l**, **m**) occurred in hot trifluoroacetic or polyphosphoric acid, but work-up as described gave no isolable products.

Crystal Data for the Lactam (**9b**).—$C_{25}H_{17}NO$, M_r = 347.42. Triclinic, space group $P\bar{1}$, a = 13.241(4), b = 9.979(5), c = 7.719(4) Å, α = 70.76(4), β = 99.91(3), γ = 116.19(3)°, V = 863.65 Å^3, $F(000)$ = 364.00, μ = 0.44 cm^{-1}, Z = 2, D_c = 1.34 g cm^{-3}, Mo-K_α radiation, λ = 0.710 69 Å.

Structure Determination.—A colourless crystal of (**9b**) *ca.* 0.5 × 0.8 × 0.3 mm^3 mounted on a fibre was used for crystallographic measurements. Intensity data were collected on a specially upgraded Hilger and Watts Y290 four-circle diffractometer. Accurate unit cell dimensions were obtained by a least-squares refinement of the values of 30 centred reflections. Intensities of 2 862 reflections were measured for $2\theta < 50°$ in a $\omega/2\theta$ scan mode. Absorption corrections were not used, but Lorentz and polarisation corrections were applied in the usual way. The measurement of 4 standard reflections every 100 reflections showed no sign of decay.

The structure was completely solved for all non-hydrogen atoms by direct methods using the Sayre tangent formula (SAYTAN) for phase determination in MULTAN86.[22] Refinement (SHELX76)[23] by full-matrix least-squares methods using the 2 262 independent reflections with $I > 2\sigma(I)$ reduced R to 0.0546 and R_w = 0.0486. Anisotropic thermal parameters were refined for all non-hydrogen atoms. All hydrogen atoms were located by a difference-Fourier map and included in the refinement. The weighting scheme used was of the form $W = 4.212/[\sigma^2(F_o) + 0.000\,185\,|F_o|^2]$.

The fractional atomic co-ordinates for non-hydrogen atoms are given in Table 2 and relevant bond lengths in Table 3. The complete lists of fractional atomic co-ordinates, bond lengths, bond angles, and anisotropic thermal parameters are deposited at the Cambridge Crystallographic Data Centre.*

* See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1990, Issue 1.

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