Synthesis of the marine dibromooxoindoline convolutamydine C

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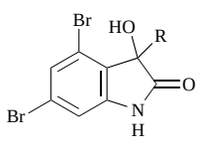
A synthesis of the marine 4,6-dibromo-3-hydroxyoxoindoline convolutamydine C 3 is described. The key steps are the rhodium(II) perfluorobutyramide catalysed cyclisation of diazoamide 17 to give the oxoindoline 18, and the subsequent high yielding one-pot hydrolysis–decarboxylation–oxidation of 19 to 20. X-Ray crystal structures have been determined for the diazoamides 10 and 17 and for the oxoindolines 11 and 13.

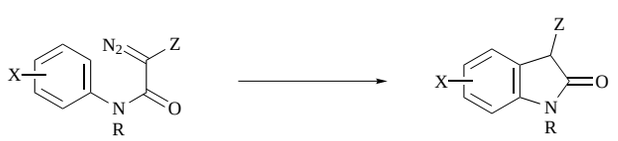
Marine organisms continue to be a rich source of interesting natural products,[1] and recently a new family of alkaloids was isolated from the Floridian bryozoan *Amathia convoluta*.[2,3] The compounds, named the convolutamydines, for example **1**–**4**, contain the novel 4,6-dibromo-3-hydroxyoxoindoline structure and only differ from each other in the nature of the second substituent at C-3. In continuation of our interest in oxoindolines,[4,5] we now report the details of the first synthesis of convolutamydine C.



1	R = CH_2COMe	convolutamydine A
2	R = CH_2CH_2Cl	convolutamydine B
3	R = Me	convolutamydine C
4	R = $CH{=}CH_2$	convolutamydine D

Results and discussion

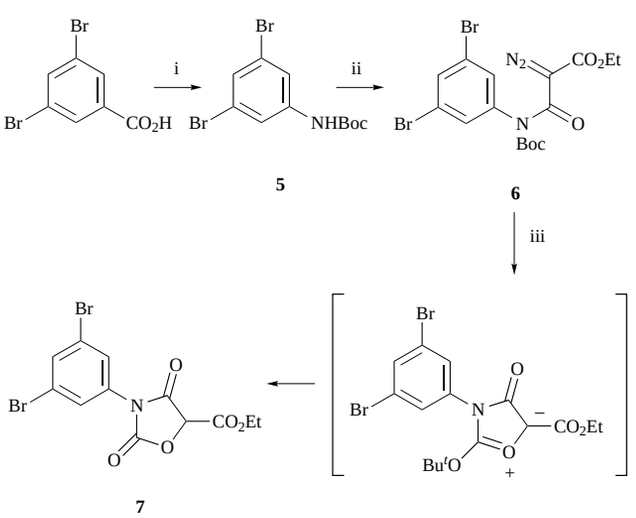
Although there are several methods for the synthesis of oxoindolines,[6] we[5] and others[7] have been interested in developing routes based on intramolecular aromatic C–H insertion reactions of rhodium carbenoids (Scheme 1).[8] In particular we have



Scheme 1

established that catalysts bearing perfluorinated carboxamide ligands are particularly effective for such processes,[5] and therefore we wished to apply this methodology to the synthesis of the dibromooxoindoline ring of the convolutamydines.

The starting material was *N*-*tert*-butoxycarbonyl-3,5-dibromoaniline **5**, readily available in high yield from 3,5-dibromobenzoic acid by reaction with diphenylphosphoryl azide (DPPA), triethylamine and *tert*-butyl alcohol in a modified Curtius rearrangement.[9] Initially we attempted to use the *tert*-butoxycarbonyl group as the *N*-protecting group for the whole synthesis and therefore the carbamate **5** was converted into the diazocarbonyl compound **6** directly by treatment of its lithium anion with ethyl diazomalonyl chloride.[5,10] However, treatment of diazo compound **6** with rhodium(II) perfluorobutyramide did not result in the desired attack on the aromatic ring to give an oxoindoline; rather attack on the *tert*-butoxy carbonyl group occurred to give, after loss of 2-methylpropene, the oxazolidinedione **7** as the sole product (by ^{1}H NMR spectroscopy) in 77% isolated yield (Scheme 2).[11]



Scheme 2 *Reagents and conditions:* i, DPPA, Et_3N, Bu^tOH (82%); ii, Bu^nLi, THF, −78 °C, then EtO_2CCN_2COCl (46%; 100% based on unconsumed **5**); iii, cat. $Rh_2(NHCOC_3F_7)_4$, CH_2Cl_2 (77%)

Given the failure of the *N*-*tert*-butoxycarbonyldiazoamide **6** to cyclise to the aromatic ring upon treatment with a rhodium(II) catalyst, an alternative *N*-protecting group was investigated. Hence the *N*-benzyldiazoamide **10** was prepared as shown in Scheme 3. Diazoamide **10** is highly crystalline and its structure was confirmed by X-ray crystallography (Fig. 1);[12] the structure shows that, in common with related diazoamides,[5] the diazo group adopts a conformation in which it is *syn* to the amide carbonyl and *anti* to the ester carbonyl, thereby placing the diazo carbon towards the *N*-aryl group. Treatment of diazoamide **10** with a catalytic amount of rhodium(II) perfluorobutyramide resulted in intramolecular attack upon the aromatic ring and formation of the oxoindoline **11** in 98% yield (Scheme 3). The structure of oxoindoline **11** was confirmed by X-ray crystallography (Fig. 2).[12] Oxoindoline **11** was cleanly *C*-methylated to give **12**. With the intention of removing the 3-ester group by hydrolysis and decarboxylation with subsequent oxidation in a separate step of the resulting 3-methyloxoindoline, ideally by air oxidation,[13] ester **12** was

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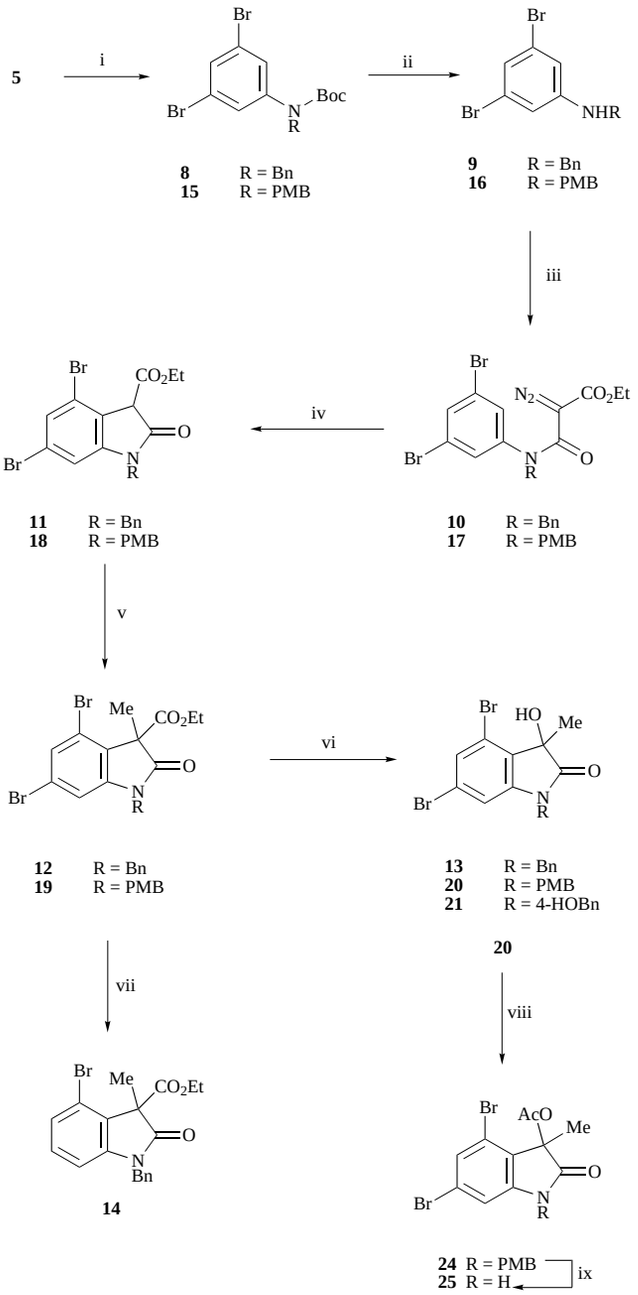


Scheme 3 *Reagents and conditions:* i, NaH, DMF, $ArCH_2X$; ii, CF_3CO_2H, CH_2Cl_2 (69% from 3,5-dibromobenzoic acid/77% from **5**); iii, EtO_2CCN_2COCl, Et_3N (61%/66%); iv, cat. $Rh_2(NHCOC_3F_7)_4$, CH_2Cl_2 (98%/99%); v, NaH, DMF, MeI (68%/66%); vi, NaOH, air, aq. THF (99%/99%) [the first yield quoted refers to the *N*-benzyl derivative; the second to the *N*-(4-methoxybenzyl) derivative]; vii, H_2–$PdCl_2$, HOAc, EtOAc (30%); viii, Ac_2O, Et_3N, DMAP, CH_2Cl_2 (99%); ix, CAN, aq. MeCN (82%)

heated in aqueous alkali in air. Under these conditions, not only was the ester group removed, but also the hydroxy group was introduced, to give the desired *N*-protected natural product, the 3-hydroxyoxoindoline **13** in 99% yield (Scheme 3). The structure of this key oxoindoline **13** was confirmed by X-ray crystallography (Fig. 3).[12] The ease of the decarboxylative oxidation of oxoindoline **12** is remarkable; in a related example of such an aerial oxidation to give a 3-hydroxyoxoindole,[13a] the 3-position already contains a hydrogen, *i.e.* no prior hydrolysis–decarboxylation is necessary, although there is an example of a hydrolysis–decarboxylation–oxidation sequence (55%) in pyrroloquinolines.[13b] Related oxidations of oxoindoles to the 3-hydroxy derivatives usually require conditions such as oxygen–Rose Bengal–NaOMe.[14]

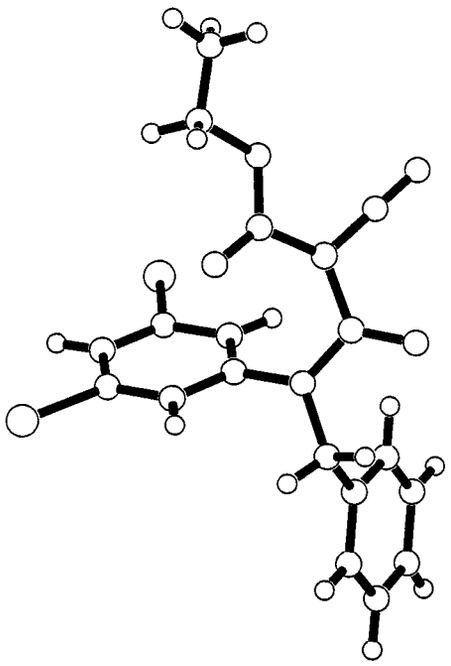


Fig. 1 X-Ray crystal structure of the diazoamide **10**

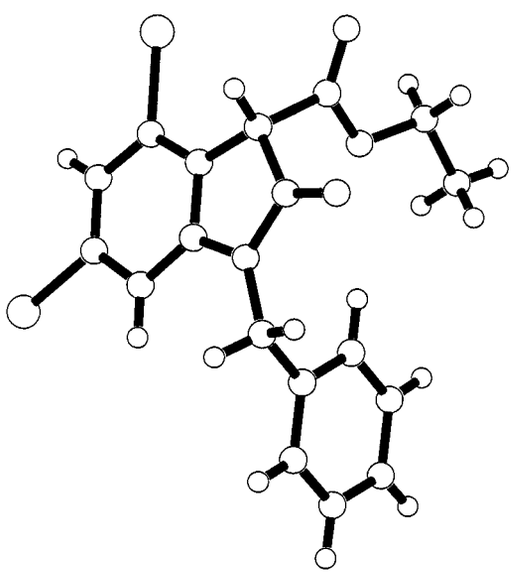


Fig. 2 X-Ray crystal structure of the oxoindoline-3-carboxylate **11**

All attempts to debenzylate oxoindoline **13** using either Li–NH_3,[15] aluminium chloride[16] or trifluoroacetic acid[17] were unsuccessful. Likewise attempts to debenzylate the ester **12** using formic acid[18] or catalytic hydrogenation[19] also failed. In the latter case, slow selective mono-debromination at C-6 occurred to give ethyl 1-benzyl-4-bromo-3-methyl-2-oxoindoline-3-carboxylate **14**.

With the failure to remove the *N*-benzyl protecting group, the sequence was repeated using the more labile *p*-methoxybenzyl (PMB) group (Scheme 3). Thus the carbamate **5** was converted into the diazoamide **17** by an analogous route; again the diazoamide **17** was highly crystalline and its X-ray crystal structure (Fig. 4) showed a very similar conformation to the diazoamide **10**.[12] Diazoamide **17** was converted into the 3-hydroxyoxoindoline **20** without incident, with the decarboxylative oxidation step again proceeding in excellent yield (Scheme 3). Frustratingly all attempts to remove the PMB group from **20** under oxidative conditions using ceric ammonium nitrate (CAN) were unsuccessful;[20] likewise oxidation of the corresponding *N*-(4-hydroxybenzyl) derivative **21**, readily obtained by boron tribromide demethylation of **20**, with DDQ[21] did not result in

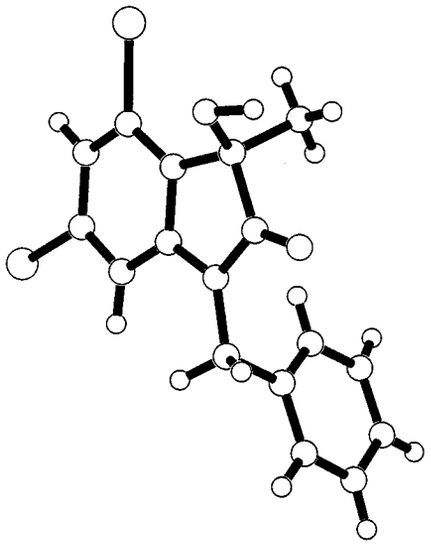


Fig. 3 X-Ray crystal structure of the 3-hydroxyoxoindoline **13**

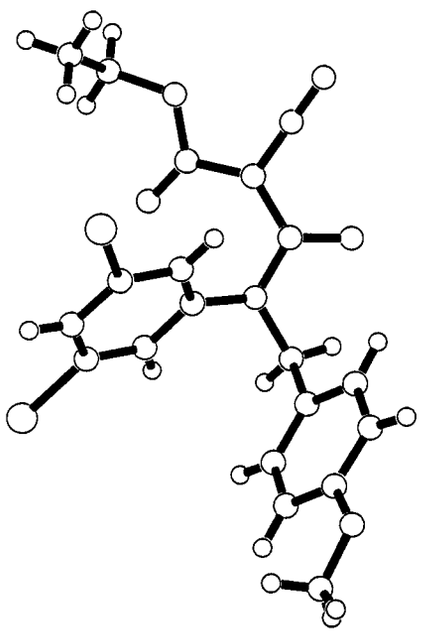
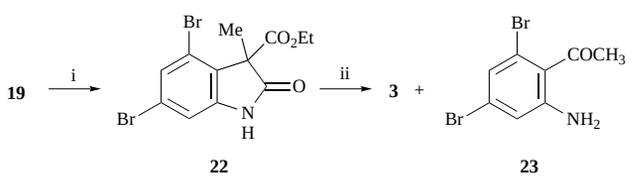


Fig. 4 X-Ray crystal structure of the diazoamide **17**



Scheme 4 *Reagents and conditions:* i, CAN, aq. MeCN (95%); ii, NaOH, air, aq. THF (18% of **3** + 63% of **23**)

N-deprotection. However, treatment of the oxoindoline **19** with CAN did result in clean removal of the PMB group, and gave the oxoindoline **22** in 95% yield (Scheme 4). However, as expected, the decarboxylative oxidation of **22** proved much more difficult than with the *N*-protected derivative **20**. Nevertheless the desired oxidation did proceed to give convolutamydine C **3** in 18% yield, although the major product was the acetophenone **23** resulting from further hydrolysis and oxidation under the reaction conditions.

In view of the poor yield of the natural product, an alternative route incorporating additional protection–deprotection steps was adopted. Thus the tertiary alcohol **20** was protected (99%) as its acetate **24** by treatment with acetic anhydride under standard conditions. Oxidative removal of the PMB group with cerium ammonium nitrate proceeded smoothly in 82% yield to give *O*-acetyl convolutamydine C **25** (Scheme 3). Finally hydrolysis of the acetate gave convolutamydine C **3** in 91% yield.

Since the submission of this manuscript, a synthesis of convolutamydine A has appeared (S. J. Garden, J. C. Torres, A. A. Ferreira, R. B. Silva and A. C. Pinto, *Tetrahedron Lett.*, 1997, **38**, 1501).

Experimental

Commercially available reagents were used throughout without further purification; solvents were dried by standard procedures. Ether refers to diethyl ether and light petroleum to the fraction with bp 40–60 °C. Analytical thin layer chromatography was carried out using aluminium-backed plates coated with Merck Kieselgel 60 GF_{254}. Plates were visualised under UV light (at 254 and/or 360 nm). Flash chromatography was carried out using Merck Kieselgel 60 H silica or Matrex silica 60. Fully characterised compounds were chromatographically homogeneous. IR spectra were recorded in the range 4000–600 cm^{-1} using a Nicolet FT-205 spectrometer, with internal calibration. ^{1}H and ^{13}C spectra were recorded in deuteriochloroform (unless otherwise stated) using Bruker AC-250 and Bruker DPX-400 instruments: *J* values were recorded in Hz. High and low resolution mass spectra were recorded on a Kratos MS80 instrument and at the EPSRC Mass Spectrometry Service at Swansea. In the mass spectra of dibromo compounds, the molecular ion is taken as the $^{79}Br^{81}Br$ peak unless otherwise stated.

3,5-Dibromo-*N*-(*tert*-butoxycarbonyl)aniline 5

A mixture of 3,5-dibromobenzoic acid (4.94 g, 17.65 mmol), triethylamine (2.56 ml, 18.34 mmol) and diphenylphosphoryl azide (5.05 g, 17.65 mmol) in *tert*-butyl alcohol (30 ml) was heated under reflux for 18 h. The mixture was cooled and concentrated under reduced pressure to give a viscous yellow oil which was taken up in dichloromethane (200 ml) and washed with aqueous sodium hydroxide (10%; 200 ml), water (2 × 200 ml) and brine (200 ml). Drying over $MgSO_4$ followed by concentration under reduced pressure afforded the crude product which could be used without further purification, or purified by flash chromatography on silica gel (9:1 then 7:1 light petroleum–ether) to give the *title compound* **5** (5.08 g, 82%) as a crystalline, colourless solid, mp 112 °C (*n*-pentane) (Found: C, 37.5; H, 3.5; N, 3.85. $C_{11}H_{13}Br_2NO_2$ requires C, 37.6; H, 3.7; N, 4.0%) (Found: M^+, 350.9296. $C_{11}H_{13}Br_2NO_2$ requires *M*, 350.9294); $\nu_{max}(CHCl_2)/cm^{-1}$ 3423, 3057, 1735, 1513 and 1154; δ_H(250 MHz; $CDCl_3$) 1.51 (9H, s), 6.49 (1H, br s), 7.31 (1H, t, *J* 1.6) and 7.51 (2H, d, *J* 1.6); δ_C(100.6 MHz; $CDCl_3$) 28.23 (CH_3), 81.55 (C), 119.90 (CH), 123.04 (C), 128.39 (CH), 140.62 (C) and 152.02 (C=O); *m*/*z* 351 (M^+, 2%), 295 (4), 251 (7) and 57 (100).

Ethyl 2-diazo-3-(3,5-dibromo-*N*-*tert*-butoxycarbonylanilino)-3-oxopropionate 6

A solution of the carbamate **5** (0.500 g, 1.42 mmol) in dry THF (12.5 ml) was cooled to −78 °C and then treated with Bu^nLi (1.6 M in hexanes; 0.99 ml, 1.58 mmol). The resulting mixture was stirred at −78 °C for 20 min and then treated dropwise with ethyl 2-diazomalonyl chloride (0.280 g, 1.58 mmol) and stirring maintained for a further 2 h. The reaction was then quenched with water (10 ml) and allowed to warm to room temperature. The organic layer was set aside and the aqueous extracted with ether (20 ml) and dichloromethane (20 ml). The organic extracts were combined, washed with brine (20 ml) and dried over $MgSO_4$ before preadsorbing on silica and subjecting to flash chromatography to give recovered starting carbamate **5** (0.269 g, 54%) and the *title compound* **6** (0.317 g, 46%) as a colourless solid, mp 63–65 °C (Found: MH^+, 491.9588.

$C_{12}H_{18}Br_2N_3O_5$ requires *M*, 491.9594); $\nu_{max}(CHCl_3)/cm^{-1}$ 2985, 2142, 1731, 1663, 1373, 1152 and 1071; δ_H(250 MHz; $CDCl_3$) 1.34 (3H, t, *J* 7.1), 1.44 (9H, s), 4.31 (2H, q, *J* 7.1), 7.36 (2H, d, *J* 1.6) and 7.63 (1H, t, *J* 1.6); δ_C(100.6 MHz; $CDCl_3$) 14.36 (CH_3), 27.84 (CH_3), 61.95 (CH_2), 84.36 (C), 122.48 (C), 130.43 (CH), 133.66 (CH), 140.11 (C), 151.32 (C=O), 160.63 (C=O) and 164.61 (C=O); *m*/*z* 492 (MH^+, <1%), 464 (M − N_2, <1%), 407 (18), 392 (12), 335 (10), 291 (8), 262 (16) and 57 (100).

Ethyl 3-(3,5-dibromophenyl)-2,4-dioxo-4,5-dihydrooxazole-5-carboxylate 7

A solution of the diazoamide **6** (0.032 g, 0.065 mmol) in dichloromethane (2 ml) was treated with rhodium(II) perfluorobutyramide (1 mg, 1 mol%) and the mixture was stirred for 2 h. When all the diazoamide had been consumed (^{1}H NMR spectroscopy) the mixture was filtered through Celite, concentrated under reduced pressure to give an oil, which was triturated with *n*-pentane–ether and recrystallised to give the *title compound* **7** (20 mg, 77%), mp 109–110 °C (*n*-pentane–ether) (Found: C, 35.0; H, 2.0; N, 3.3. $C_{12}H_9Br_2NO_5$ requires C, 35.4; H, 2.2; N, 3.4%) (Found: M^+, 406.8823. $C_{12}H_9Br_2NO_5$ requires *M*, 406.8829); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2987, 1838, 1755, 1566, 1447, 1338, 1191, 1168 and 1105; δ_H(250 MHz; $CDCl_3$) 1.39 (3H, t, *J* 7.1), 4.40 (2H, q, *J* 7.1), 5.38 (1H, s), 7.63 (2H, t, *J* 1.6) and 7.75 (1H, t, *J* 1.6); δ_C(100.6 MHz; $CDCl_3$) 14.02 (CH_3), 64.04 (CH_2), 76.50 (CH), 123.24 (C), 127.05 (CH), 132.23 (C), 134.98 (CH), 152.03 (C=O), 161.79 (C=O) and 164.29 (C=O); *m*/*z* 407 (M^+, 13%), 335 (8), 278 (10), 170 (9), 57 (13) and 29 (100).

***N*-Benzyl-3,5-dibromo-*N*-(*tert*-butoxycarbonyl)aniline 8**

A solution of crude carbamate **5** (3.06 g, 8.72 mmol) in DMF (18 ml) was added to a suspension of sodium hydride (60% dispersion in mineral oil; 0.384 g, 9.59 mmol) in DMF (18 ml) whilst cooling in an ice bath, and the resulting mixture was stirred for 4 h, then treated with benzyl bromide (1.491 g, 8.72 mmol). After stirring for a further 0.5 h, the mixture was quenched with water (180 ml) and extracted with ether (1 × 180 ml, 2 × 90 ml). The ether extracts were combined and washed with brine (2 × 90 ml), dried over $MgSO_4$ and concentrated under reduced pressure to give the crude *title compound* **8** as a pale yellow solid (≈3.85 g) which was taken on to the next step without purification. A sample was recrystallised to give a colourless solid, mp 64–65 °C (light petroleum) (Found: C, 49.0; H, 4.3; N, 3.2. $C_{18}H_{19}Br_2NO_2$ requires C, 48.9; H, 4.2; N, 3.4%) (Found: M^+, 440.9764. $C_{18}H_{19}Br_2NO_2$ requires *M*, 440.9764); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2981, 1702, 1583 and 1158; δ_H(400 MHz; $CDCl_3$) 1.43 (9H, s), 4.80 (2H, s), 7.35–7.15 (7H, m) and 7.44 (1H, t, *J* 1.6); δ_C(100.6 MHz; $CDCl_3$) 28.18 (CH_3), 53.65 (CH_2), 81.59 (C–O), 122.24 (C), 127.13 (CH), 128.09 (CH), 128.62 (CH), 131.20 (CH), 137.69 (C), 144.95 (C) and 153.95 (C=O); *m*/*z* 441 (M^+, 1%), 341 (25), 277 (21), 91 (100) and 57 (43).

***N*-Benzyl-3,5-dibromoaniline 9**

A solution of the crude carbamate **8** (≈3.85 g, 8.72 mmol) in dichloromethane (30 ml), cooled in an ice bath was treated with trifluoroacetic acid (30 ml). The mixture was stirred at room temperature for 16 h then concentrated under reduced pressure, diluted with dichloromethane (50 ml) and washed with aqueous sodium hydroxide (2 M; 50 ml). The aqueous layer was extracted with dichloromethane, the organic extracts were combined and washed with water (50 ml) and brine (50 ml). The solution was dried (Na_2SO_4), preadsorbed onto silica and subjected to flash chromatography and crystallisation to afford the *title compound* **9** (2.061 g, 69% from 3,5-dibromobenzoic acid) as large yellow prisms, mp 60–61 °C (*n*-pentane–ether) (Found: C, 45.5; H, 3.0; N, 4.2. $C_{13}H_{11}Br_2N$ requires C, 45.5; H, 3.25; N, 4.1%) (Found: M^+, 340.9246. $C_{13}H_{11}Br_2N$ requires *M*, 340.9240); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3445, 3422, 2860, 1590, 1496, 1358, 1109, 1089, 1070, 981 and 822; δ_H(250 MHz; $CDCl_3$) 4.12 (1H, br s), 4.26 (2H, d, *J* 5.3), 6.67 (2H, d, *J* 1.6), 6.96 (1H, t, *J* 1.6) and 7.40–7.24 (5H, m); δ_C(100.6 MHz; $CDCl_3$) 48.33, 114.69, 123.05, 123.88, 127.85, 128.06, 129.23, 138.41 and 150.42; *m*/*z* 341 (M^+, 11%), 91 (100) and 28 (53).

Ethyl 2-diazo-3-(*N*-benzyl-3,5-dibromoanilino)-3-oxopropionate 10

A solution of *N*-benzyl-3,5-dibromoaniline **9** (0.240 g, 5.57 mmol) in dichloromethane (80 ml) was treated with triethylamine (1.24 g, 12.26 mmol, 1.71 ml) and ethyl 2-diazomalonyl chloride (0.984 g, 5.57 mmol). The mixture was stirred at room temperature for 4 h, and then heated under reflux for 40 min. The solution was allowed to cool, preadsorbed onto silica and subjected to flash chromatography (9:1 then 8:1 light petroleum–ether) to give recovered starting aniline **9** (0.649 g, 34%) and the *title compound* **10** (1.625 g, 61%) as a bright yellow crystalline solid, mp 119–120 °C (light petroleum–ether) (Found: C, 44.7; H, 2.95; N, 8.7. $C_{18}H_{15}Br_2N_3O_3$ requires C, 44.9; H, 3.1; N, 8.7%) (Found: MH^+, 479.9558. $C_{18}H_{15}Br_2N_3O_3$ requires *M*, 479.9558); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2134, 1719, 1580 and 1374; δ_H(250 MHz; $CDCl_3$) 1.15 (3H, t, *J* 7.1), 4.04 (2H, q, *J* 7.1), 4.97 (2H, s), 7.22 (2H, d, *J* 1.6), 7.40–7.24 (5H, m) and 7.49 (1H, t, *J* 1.6); δ_C(100.6 MHz; $CDCl_3$) 14.58 (CH_3), 54.87 (NCH_2), 62.02 (OCH_2), 68.68 (C=N_2), 123.05 (C), 128.17 (CH), 128.23 (CH), 128.32 (CH), 129.09 (CH), 132.56 (CH), 136.58 (C), 145.65 (C), 161.18 (C=O) and 161.94 (C=O); *m*/*z* 480 (MH^+, 75%), 340 (10) and 108 (8).

Ethyl 1-benzyl-4,6-dibromo-2-oxoindoline-3-carboxylate 11

A solution of the diazoamide **10** (0.150 g, 0.312 mmol) in dry dichloromethane (2.6 ml) was added to a suspension of rhodium(II) perfluorobutyramide (6.6 mg, 2 mol%) in dry dichloromethane (3.8 ml) and the mixture stirred at room temperature for 0.5 h. The reaction mixture was filtered through Celite and concentrated under reduced pressure to give pure *oxoindoline* **11** (0.138 g, 98%) as a colourless solid, mp 152–153 °C (ethanol) (Found: C, 47.9; H, 3.2; N, 3.1. $C_{18}H_{15}Br_2NO_3$ requires C, 47.7; H, 3.3; N, 3.1%) (Found: MH^+, 452.9410. $C_{18}H_{15}Br_2NO_3$ requires *M*, 452.9400); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1751, 1742 and 1605; δ_H(250 MHz; $CDCl_3$) 1.13 (3H, t, *J* 7.1), 4.30 (2H, m), 4.43 (1H, s), 4.78 (1H, d, *J* 15.8), 4.97 (1H, d, *J* 15.8), 6.80 (1H, d, *J* 1.35) and 7.40–7.20 (6H, m); δ_C(100.6 MHz; $CDCl_3$) 14.09 (CH_3), 44.38 (NCH_2), 54.10 (CH), 62.59 (OCH_2), 111.84 (CH), 120.05, 123.37, 123.74, 127.06 (CH), 127.30 (CH), 128.10 (CH), 128.43 (CH), 129.05 (CH), 134.36 (C), 146.12 (C), 164.80 (C=O) and 169.74 (C=O); *m*/*z* 452 (M^+, 17%), 380 (12), 110 (8) and 91 (100).

Ethyl 1-Benzyl-4,6-dibromo-3-methyl-2-oxoindoline-3-carboxylate 12

A solution of the oxoindoline **11** (0.100 g, 0.220 mmol) in dry DMF (3 ml) was added slowly to a stirred, ice-cooled suspension of sodium hydride (60% dispersion in mineral oil; 0.0096 g, 0.240 mmol) in dry DMF (2 ml) and stirred for 1 h after which time evolution of hydrogen had ceased. Iodomethane (0.035 g, 0.240 mmol, ≈15 μl) was added and stirring was continued for a further 3 h whilst allowing the reaction to reach ambient temperature. The reaction mixture was diluted with ether (20 ml) and water (20 ml). The aqueous layer was extracted with ether (20 ml then 50 ml); the combined ethereal extracts were washed with brine, dried ($MgSO_4$), concentrated under reduced pressure and subjected to flash silica gel column chromatography and recrystallisation to afford the *title compound* **12** (0.070 g, 68%) as colourless crystals, mp 99–101 °C (*n*-pentane–ether) (Found: C, 48.7; H, 3.7; N, 3.0. $C_{19}H_{17}Br_2NO_3$ requires C, 48.85; H, 3.7; N, 3.0%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1752, 1723, 1599, 1572, 1340 and 1110; δ_H(250 MHz; $CDCl_3$) 1.20 (3H, t, *J* 7.1), 1.80 (3H, s), 4.21 (2H, dq, *J* 7.1 and 2.0), 4.77 (1H, d, *J* 15.9), 5.03 (1H, d, *J* 15.9), 6.80 (1H, d, *J* 1.4) and 7.35–7.22 (6H, m); δ_C(100.6 MHz; $CDCl_3$) 14.41 (CH_3), 18.05 (CH_3), 44.45

(NCH_2), 57.00 (C), 62.75 (OCH_2), 112.28 (CH), 119.45 (C), 123.17 (C), 127.26 (CH), 128.41 (CH), 129.24 (CH), 129.38 (CH), 130.05 (C), 134.90 (C), 145.79 (C), 167.48 (C=O) and 174.61 (C=O); *m*/*z* 469 (M^+, 13%), 394 (28) and 91 (100).

1-Benzyl-4,6-dibromo-3-hydroxy-3-methylindolin-2-one 13

A stirred solution of the ester **12** (18 mg, 0.038 mmol) in THF–water (3:1; 3.1 ml) was treated with sodium hydroxide pellets (16 mg, 0.4 mmol) and the resulting mixture heated under reflux for 18 h under an atmosphere of air. After allowing to cool to ambient temperature, the suspension was acidified with hydrochloric acid (2 M) and the THF was removed under reduced pressure. The aqueous concentrate was extracted with ether (10 ml and 5 ml). The organic extracts were combined and washed with water (5 ml), brine (5 ml) and dried over $MgSO_4$. Concentration under reduced pressure gave pure *title compound* **13** (16 mg, 99%) as colourless prisms, mp 148–149 °C (Found: C, 46.4; H, 2.8; N, 3.2. $C_{16}H_{13}Br_2NO_2$ requires C, 46.75; H, 3.2; N, 3.4%) (Found: M^+, 410.9296. $C_{16}H_{13}Br_2NO_2$ requires *M*, 410.9294); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3567, 1735, 1600, 1574, 1344, 1164, 1036, 937 and 839; δ_H(250 MHz; $CDCl_3$) 1.80 (3H, s), 2.67 (1H, br s; removed by D_2O exchange), 4.8 (1H, d, *J* 15.8), 4.90 (1H, d, *J* 15.8), 6.80 (1H, d, *J* 1.6) and 7.38–7.20 (6H, m); δ_C(100.6 MHz; $CDCl_3$) 21.71 (CH_3), 43.05 (CH_2), 73.96 (C), 111.16 (CH), 118.81 (C), 122.68 (C), 126.21 (CH), 127.23 (CH), 127.50 (C), 128.20 (CH), 128.48 (CH), 133.64 (C), 143.93 (C) and 176.46 (C=O); *m*/*z* 411 (M^+, 14%), 302 (7), 155 (7), 113 (7), 91 (100) and 57 (18).

Ethyl 1-benzyl-4-bromo-3-methyl-2-oxoindoline-3-carboxylate 14

A solution of the oxoindoline **12** (0.036 g, 0.0077 mmol) in ethyl acetate–acetic acid (4:1; 5 ml) was treated with $PdCl_2$ (0.0087 g, 0.049 mmol) and the resulting suspension stirred under an atmosphere of hydrogen gas. The reaction was monitored by TLC; after 3 h further $PdCl_2$ (0.0168 g) was added and the mixture stirred for 18 h under hydrogen. The resulting suspension was filtered through Celite, washed with saturated aqueous $NaHCO_3$, water and brine. After drying over $MgSO_4$, the mixture was preadsorbed onto silica and subjected to flash chromatography to give unreacted starting oxoindoline **12** (0.025 g, 69%) and the *title compound* **14** (0.009 g, 30%) as a sticky solid (Found: M^+, 387.0469. $C_{19}H_{18}{}^{79}BrNO_3$ requires *M*, 387.04705); $\nu_{max}(CHCl_3)/cm^{-1}$ 1750, 1717, 1605, 1456, 1377, 1237, 1217 and 1169; δ_H(250 MHz; $CDCl_3$) 1.20 (3H, t, *J* 7.1), 1.83 (3H, s), 4.20 (2H, dq, *J* 7.1 and 1.8), 4.81 (1H, d, *J* 15.9), 5.07 (1H, d, *J* 15.9), 6.66 (1H, dd, *J* 7.9 and 7.6), 7.06 (1H, t, *J* 7.9), 7.15 (1H, d, *J* 7.6) and 7.40–7.18 (5H, m); δ_C(100.6 MHz; $CDCl_3$) 14.41 (CH_3), 18.14 (CH_3), 44.35 (NCH_2), 57.29 (C), 62.56 (OCH_2), 108.88 (CH), 119.02 (C), 127.05 (CH), 127.31 (CH), 128.18 (CH), 129.23 (CH), 130.27 (C), 130.39 (CH), 135.43 (C), 144.84 (C), 168.06 (C=O) and 174.795 (C=O); *m*/*z* 387 (M^+, 7%), 314 (8), 155 (4), 119 (4), 91 (100) and 65 (8).

3,5-Dibromo-*N*-(*tert*-butoxycarbonyl)-*N*-(4-methoxybenzyl)-aniline 15

A solution of carbamate **5** (3.00 g, 8.55 mmol) in dry DMF (18 ml) was added to a stirred suspension of sodium hydride (60% dispersion in mineral oil; 0.376 g, 9.40 mmol) in dry DMF (18 ml) whilst cooling in an ice bath and the resulting mixture was stirred for 20 min. 4-Methoxybenzyl chloride (1.16 ml, 1.34 g, 8.55 mmol) was then added and the mixture stirred for a further 21 h. The reaction was quenched with water (180 ml) and extracted with ether (180 ml then 2 × 90 ml). The combined ether extracts were washed with brine (2 × 90 ml), dried over $MgSO_4$ and concentrated under reduced pressure to give essentially pure product as a pale yellow solid (4.03 g, 100%) used without further purification. A sample was recrystallised from light petroleum–ether to give the *title compound* **15** as colourless crystals, mp 82–84 °C (light petroleum–ether) (Found: C, 48.4; H, 4.2; N, 2.95. $C_{19}H_{21}Br_2NO_3$ requires C, 48.4; H, 4.5; N, 3.0%) (Found: M^+, 470.9871. $C_{19}H_{21}Br_2NO_3$ requires *M*, 470.9869); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3048, 2934, 2840, 1699, 1583, 1556, 1514, 1440, 1369, 1266, 1160, 1034, 909 and 858; δ_H(250 MHz; $CDCl_3$) 1.44 (9H, s), 3.80 (3H, s), 4.74 (2H, s), 6.88–6.80 (2H, m), 7.15–7.08 (2H, m), 7.26 (2H, d, *J* 1.7) and 7.44 (1H, t, *J* 1.7); δ_C(100.6 MHz; $CDCl_3$) 28.62 (CH_3), 53.44 (NCH_2), 55.65 (OCH_2), 81.85 (OC), 114.42 (CH), 122.59 (C), 128.77 (CH), 129.04 (CH), 130.10 (C), 131.64 (CH), 145.28 (C), 154.36 (C=O) and 159.39 (C); *m*/*z* 471 (M^+, 2%), 415 (20), 371 (13), 251 (8), 121 (100), 57 (74) and 41 (42).

3,5-Dibromo-*N*-(4-methoxybenzyl)aniline 16

A solution of the crude carbamate **15** (3.92 g, 8.32 mmol) in dichloromethane (30 ml) was cooled in an ice bath and treated with trifluoroacetic acid (30 ml). The mixture was stirred at room temperature for 80 min, then concentrated under reduced pressure to give an oil which was taken up in dichloromethane (50 ml) and washed with dilute aqueous sodium hydroxide (10%; 50 ml). The aqueous layer was extracted with dichloromethane (25 ml). The organic extracts were combined, washed with water (50 ml), brine (50 ml), dried over Na_2SO_4, preadsorbed onto silica and subjected to flash chromatography to give the *title compound* **16** (2.39 g, 77% for the two steps) as a colourless crystalline solid, mp 73–74 °C (*n*-pentane–ether) (Found: C, 45.1; H, 3.2; N, 3.6. $C_{14}H_{13}Br_2NO$ requires C, 45.3; H, 3.5; N, 3.8%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3423, 2840, 1590, 1560, 1514, 1264, 1176, 1034, 895 and 821; δ_H(250 MHz; $CDCl_3$) 3.81 (3H, s), 4.06 (1H, br s), 4.19 (2H, d, *J* 4.8), 6.67 (2H, d, *J* 1.6), 6.85–6.91 (2H, m), 6.96 (1H, t, *J* 1.6) and 7.27–7.20 (2H, m); δ_C(100.6 MHz; $CDCl_3$) 47.85 (CH_2), 55.71 (OCH_3), 114.65 (CH), 114.68 (CH), 122.97 (CH), 123.86 (C), 129.19 (CH), 130.39 (C), 150.45 (C) and 159.60 (C); *m*/*z* 371 (M^+, 30%), 251 (8), 121 (100) and 78 (19).

Ethyl 2-diazo-3-[3,5-dibromo-*N*-(4-methoxybenzyl)anilino]-3-oxopropionate 17

A solution of the aniline **16** (1.00 g, 2.695 mmol) in dichloromethane (39 ml) was treated with triethylamine (5.93 mmol, 0.83 ml) and ethyl 2-diazomalonyl chloride (0.476 g, 2.695 mmol); the mixture was stirred at room temperature for 70 h. The solution was washed with dilute hydrochloric acid (2 M; 50 ml), water (20 ml) and brine (20 ml). Drying over Na_2SO_4 followed by preadsorption onto silica and flash chromatography (gradient elution from 8:1 to 6:1 light petroleum–ether) gave recovered starting aniline **16** (0.30 g, 30%) and the *title compound* **17** (0.907 g, 66%) as a bright yellow crystalline solid, mp 95 °C (*n*-pentane–ether–EtOAc) (Found: C, 44.5; H, 3.05; N, 8.1. $C_{19}H_{17}Br_2N_3O_4$ requires C, 44.6; H, 3.35; N, 8.2%) (Found: M^+, 510.9567. $C_{19}H_{17}Br_2N_3O_4$ requires *M*, 510.9546); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2839, 2133, 1718, 1633, 1580, 1557, 1514, 1436, 1422, 1374, 1320 and 1107; δ_H(250 MHz; $CDCl_3$) 1.14 (3H, t, *J* 7.1), 3.78 (3H, s), 4.03 (2H, q, *J* 7.1), 4.90 (2H, s), 6.84–6.80 (2H, m), 7.18–7.14 (2H, m), 7.20 (2H, d, *J* 1.6) and 7.49 (1H, t, *J* 1.6); δ_C(100.6 MHz; $CDCl_3$) 14.21 (CH_3), 54.00 (NCH_2), 55.28 (OCH_3), 61.60 (OCH_2), 68.16 (C=N_2), 114.08 (CH), 122.64 (C), 128.18 (CH), 128.28 (C), 129.59 (CH), 132.22 (CH), 145.14 (C), 159.25 (C), 160.86 (C) and 161.46 (C); *m*/*z* 511 (M^+, <1%), 483 ($M - N_2$, 4%), 410 (9), 277 (5), 206 (35), 161 (13), 134 (11) and 121 (100).

Ethyl 4,6-dibromo-1-(4-methoxybenzyl)-2-oxoindoline-3-carboxylate 18

A solution of the diazoamide **17** (0.415 g, 0.812 mmol) in dry dichloromethane (18 ml) was treated with rhodium(II) perfluorobutyramide (0.0086 g, 1 mol%) and the mixture stirred at room temperature for 1.5 h. The reaction mixture was rapidly filtered through Celite and concentrated under reduced pressure to give pure *title compound* **18** (0.390 g, 99%) as an unstable colourless foam/solid (Found: M^+, 482.9496. $C_{19}H_{17}Br_2NO_4$

requires *M*, 482.9506); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2987, 2939, 2840, 1750, 1723, 1605, 1515, 1250, 1178, 1157, 1034 and 836; δ_H(250 MHz; $CDCl_3$) 1.31 (3H, t, *J* 7.1), 3.79 (3H, s), 4.29 (2H, dq, *J* 7.1 and 2.5), 4.41 (1H, s), 4.72 (1H, d, *J* 15.6), 4.89 (1H, d, *J* 15.6), 6.82 (1H, d, *J* 1.3), 6.86 (2H, d, *J* 8.7), 7.20 (2H, d, *J* 8.7) and 7.34 (1H, d, *J* 1.3); δ_C(100.6 MHz; $CDCl_3$) 13.93 (CH_3), 43.71 (NCH_2), 53.90 (CH), 55.13 (OCH_3), 62.04 (OCH_2), 111.69 (CH), 114.24 (CH), 119.82 (C), 123.15 (C), 123.55 (C), 126.18 (C), 128.16 (CH), 128.34 (CH), 145.93 (C), 159.21 (C), 164.68 (C=O) and 169.52 (C=O); *m*/*z* 483 (M^+, 1%), 121 (100), 78 (6), 45 (13) and 31 (29).

Ethyl 4,6-dibromo-1-(4-methoxybenzyl)-3-methyl-2-oxoindoline-3-carboxylate 19

A solution of the oxoindoline **18** (0.390 g, 0.808 mmol) in dry DMF (12 ml) was added slowly to a stirred, ice-cooled suspension of sodium hydride (60% dispersion in mineral oil; 0.036 g, 0.890 mmol) in dry DMF (18 ml) and stirring was maintained for 0.5 h, when evolution of hydrogen subsided. Then iodomethane (0.126 g, 0.890 mmol, ≈55.5 μl) was added and stirring was continued for a further 3 h whilst allowing the reaction to reach ambient temperature. The reaction mixture was diluted with ether (120 ml) and water (120 ml). The aqueous layer was extracted with ether (120 ml then 300 ml); the combined ethereal extracts were washed with brine, dried ($MgSO_4$), concentrated under reduced pressure and subjected to flash chromatography on silica gel to yield the *title compound* **19** (0.265 g, 66%) as a colourless oil which crystallised on cooling, mp 120–120.5 °C (*n*-pentane) (Found: C, 48.3; H, 3.7; N, 2.8. $C_{20}H_{19}Br_2NO_4$ requires C, 48.3; H, 3.7; N, 2.8%) (Found: M^+, 496.9665. $C_{20}H_{19}Br_2NO_4$ requires *M*, 496.9662); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1752, 1723, 1600, 1515, 1112 and 838; δ_H(250 MHz; $CDCl_3$) 1.20 (3H, t, *J* 7.1), 1.79 (3H, s), 3.79 (3H, s), 4.20 (2H, dq, *J* 7.1 and 2.0), 4.77 (1H, d, *J* 15.9), 5.03 (1H, d, *J* 15.9), 6.82 (1H, d, *J* 1.4), 6.86 (2H, d, *J* 8.6), 7.18 (2H, d, *J* 8.6) and 7.31 (1H, d, *J* 1.4); δ_C(100.6 MHz; $CDCl_3$) 14.40 (CH_3), 18.03 (CH_3), 44.00 (NCH_2), 55.68 (OCH_3), 56.99 (C), 62.68 (OCH_2), 112.32 (CH), 114.79 (CH), 119.39 (C), 123.125 (C), 126.93 (C), 128.71 (CH), 129.13 (CH), 129.38 (C), 129.33 (C), 145.84 (C), 159.765 (C), 167.49 (C=O) and 174.56 (C=O); *m*/*z* 497 (M^+, 22%), 304 (4), 121 (100), 91 (10) and 78 (16).

4,6-Dibromo-3-hydroxy-1-(4-methoxybenzyl)-3-methylindolin-2-one 20

A stirred solution of the ester **19** (0.245 g, 0.493 mmol) in THF–water (3:1; 40 ml) was treated with sodium hydroxide pellets (0.203 g, 5.075 mmol) and the resulting mixture heated under reflux for 21 h under an atmosphere of air. After allowing the mixture to cool to ambient temperature, the suspension was acidified carefully with aqueous hydrochloric acid (2 M) and the THF was removed under reduced pressure. The aqueous concentrate was extracted with ether (60 ml and 30 ml). The organic extracts were combined, washed with water (60 ml), brine (30 ml) and dried over $MgSO_4$. Concentration under reduced pressure gave the *title compound* **20** (0.214 g, 99%) as an amorphous, colourless solid, mp 168–169 °C (Found: C, 46.3; H, 3.1; N, 2.9. $C_{17}H_{15}Br_2NO_3$ requires C, 46.3; H, 3.4; N, 3.2%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3413, 2934, 2840, 1735, 1601, 1574, 1514, 1343, 1161 and 1034; δ_H(250 MHz; $CDCl_3$) 1.79 (3H, s), 2.67 (1H, br s), 3.79 (3H, s), 4.72 (1H, d, *J* 15.5), 4.86 (1H, d, *J* 15.5), 6.83 (1H, d, *J* 1.5), 6.86 (2H, m), 7.18 (2H, m) and 7.34 (1H, d, *J* 1.5); δ_C(100.6 MHz; $CDCl_3$) 22.97 (CH_3), 43.82 (NCH_2), 75.26 (C), 112.48 (CH), 114.85 (CH), 120.02 (C), 123.96 (C), 126.85 (C), 128.67 (C), 128.92 (CH), 129.96 (CH), 145.17 (C), 159.77 (C) and 177.66 (C=O); *m*/*z* 441 (M^+, 6%), 320 (1), 155 (2) and 121 (100).

4,6-Dibromo-3-hydroxy-1-(4-hydroxybenzyl)-3-methylindolin-2-one 21

The oxoindoline **20** (0.052 g, 0.118 mmol) was taken up in dry dichloromethane (1 ml) and the solution was cooled to −80 °C in a dry ice–acetone bath, then treated slowly with BBr_3 (1 M solution in dichloromethane; 0.37 ml, 0.37 mmol). The mixture was stirred for 16 h whilst allowing to warm slowly to 8 °C; water and dichloromethane (5 ml) were added and the suspension stirred. The organic layer was washed twice with water and dried ($MgSO_4$). Concentration under reduced pressure yielded the *title compound* **21** (0.050 g, 99%) as a colourless solid, mp 167 °C (*n*-pentane–light petroleum–ethyl acetate) (Found: M^+, 426.9245. $C_{16}H_{13}Br_2NO_3$ requires *M*, 426.9244); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3686, 3576, 2930, 1735, 1601, 1516, 1162 and 839; δ_H(250 MHz; $CDCl_3$) 1.78 (3H, s), 2.85 (1H, br s), 4.72 (1H, d, *J* 15.6), 4.81 (1H, d, *J* 15.6), 5.25 (1H, br s), 6.78 (2H, m), 6.82 (1H, d, *J* 1.5), 7.11 (2H, m) and 7.34 (1H, d, *J* 1.5); δ_C(100.6 MHz; $CDCl_3$) 22.84 (CH_3), 43.86 (CH_2), 75.38 (C), 112.56 (CH), 116.38 (CH), 120.07 (C), 123.99 (C), 126.73 (C), 128.67 (C), 129.05 (CH), 129.84 (CH), 145.03 (C), 155.96 (C) and 178.00 (C=O); *m*/*z* 427 (M^+, <1%), 121 (100) and 78 (5).

Ethyl 4,6-dibromo-3-methyl-2-oxoindoline-3-carboxylate 22

The oxoindoline **19** (0.050 g, 0.101 mmol) was dissolved in acetonitrile (1.21 ml) and water (0.40 ml) was added. The solution was treated with ceric ammonium nitrate (0.221 g, 0.402 mmol), stirred for 2.5 h, poured into water and extracted with ethyl acetate (2 × 10 ml; brine was added to help clear emulsions). The organic extracts were combined, washed with water, brine and dried ($MgSO_4$). Preadsorption on silica followed by flash column chromatography gave the *title compound* **22** (0.036 g, 95%) as a colourless powder, mp 175–176 °C (*n*-pentane–ethyl acetate) (Found: C, 37.9; H, 2.8; N, 4.0. $C_{12}H_{11}Br_2NO_3$ requires C, 38.2; H, 2.9; N, 3.7%) (Found: M^+, 376.9092. $C_{12}H_{11}Br_2NO_3$ requires *M*, 376.9087); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3417, 2959, 1755, 1735, 1610, 1426 and 1112; δ_H(250 MHz; $CDCl_3$) 1.20 (3H, t, *J* 7.15), 1.77 (3H, s), 4.10–4.30 (2H, m), 7.06 (1H, d, *J* 1.5), 7.36 (1H, d, *J* 1.5) and 8.07 (1H, br s); δ_C(100.6 MHz; $CDCl_3$) 14.12 (CH_3), 57.46 (C), 62.84 (CH_2), 113.13 (CH), 119.62 (C), 123.21 (C), 129.28 (CH), 129.86 (C), 143.65 (C), 167.38 (C=O) and 176.3 (C=O); *m*/*z* 377 (M^+, 15%), 304 (100), 223 (30), 195 (13), 155 (33), 116 (24), 89 (23) and 29 (81).

Convolutamydine C 3

A stirred solution of the ester **22** (0.0240 g, 0.0637 mmol) in THF–water (3:1; 5 ml) was treated with sodium hydroxide pellets (0.025 g, 0.610 mmol), and the resulting mixture heated under reflux for 50 h under an atmosphere of oxygen. After allowing to cool to ambient temperature, the suspension was acidified carefully with aqueous hydrochloric acid (2 M) and the THF was removed under reduced pressure. The aqueous concentrate was extracted with ether (2 × 10 ml). The organic extracts were combined and washed with water, brine and dried ($MgSO_4$). Preadsorption on silica, followed by flash column chromatography (3:1 then 2:1 light petroleum–EtOAc) gave (i) the title compound **3** as a colourless solid (2.4 mg, 18%), mp >160 °C (decomp.) (light petroleum–ethyl acetate) (lit.,[3] 175–180 °C from acetone) (Found: M^+, 318.8844. Calc. for $C_9H_7{}^{79}Br{}^{79}BrNO_2$: *M*, 318.8845) (Found: M^+, 320.8829. Calc. for $C_9H_7{}^{79}Br{}^{81}BrNO_2$: *M*, 320.8825); $\nu_{max}(CHCl_3)/cm^{-1}$ 3691, 3607, 2928, 1749 and 1602; δ_H(250 MHz; $CDCl_3$) 1.76 (3H, s, Me), 2.67 (1H, br, OH), 7.00 (1H, d, *J* 1.5), 7.38 (1H, d, *J* 1.5) and 7.45 (1H, NH); δ_C(100.6 MHz; [$^2H_6$]acetone) 19.9 (Me), 73.0 (C3), 110 (C7), 118.3 (C6), 121.1 (C4), 126.5 (C5), 143.3 (C7a) and 176.9 (C2); C3a not observed; *m*/*z* 321 (M^+, 24%), 306 (38), 278 (33), 170 (11), 90 (19), 74 (12), 63 (29) and 43 (100); and (ii) 2-amino-4,6-dibromoacetophenone **23** as a pale yellow solid (10.0 mg, 63%), mp 89–91 °C (Found: M^+, 292.8877. $C_8H_7Br_2NO$ requires *M*, 292.8876); $\nu_{max}(CHCl_3)/cm^{-1}$ 3502, 3399, 3093, 3011, 2928, 2856, 1680, 1604, 1581, 1539, 1409, 1355 and 1253; δ_H(250 MHz; $CDCl_3$) 2.63 (3H, s), 4.68 (2H, br s, exchangeable with D_2O), 6.80 (1H, d, *J* 1.7) and 7.09 (1H, d, *J* 1.7); δ_C(100.6 MHz; $CDCl_3$) 32.4 (CH_3), 118.8

(CH), 121.6 (C), 125.2 (CH), 125.4 (C), 147.8 (C) and 203.9 (C=O); *m*/*z* 293 (M^+, 8%), 278 (100), 250 (5), 170 (8), 90 (5), 63 (17) and 43 (37).

4,6-Dibromo-1-(4-methoxybenzyl)-3-methyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl acetate 24

Tertiary alcohol **20** (0.025 g, 0.057 mmol) was taken up in dry dichloromethane (2 ml) and treated with triethylamine (≈0.024 g, 0.24 mmol), acetic anhydride (≈0.015 g, 0.14 mmol), along with a catalytic amount of 4-dimethylaminopyridine. After stirring at room temperature for 25 h the solvent was removed under reduced pressure. The residue was taken up in ether (10 ml), washed sequentially with hydrochloric acid (2 M; 2 × 5 ml), water and brine. The ether solution was dried ($MgSO_4$), filtered, then concentrated under reduced pressure to yield the title compound **24** (0.028 g, 99%) as an oily, colourless solid which was used directly without crystallisation (Found: M^+, 482.9519. $C_{19}H_{17}Br_2NO_4$ requires *M*, 482.9506); ν_{max}(film)/cm^{-1} 3081, 2998, 2934, 2837, 1739, 1602, 1515, 1164, 1105, 1043 and 734; δ_H(250 MHz; $CDCl_3$) 1.74 (3H, s), 2.14 (3H, s), 3.79 (3H, s), 4.75 (1H, d, *J* 15.7), 4.93 (1H, d, *J* 15.7), 6.76 (1H, d, *J* 1.5), 6.88 (2H, m) and 7.20–7.36 (3H, m); δ_C(100.6 MHz; $CDCl_3$) 20.01 (CH_3), 20.60 (CH_3), 43.64 (CH_2), 55.27 (CH_3), 77.62 (C), 112.13 (CH), 114.38 (CH), 117.83 (C), 123.46 (C), 126.28 (C), 126.50 (C), 128.48 (CH), 128.81 (CH), 144.89 (C), 159.30 (C), 169.20 (C=O) and 174.48 (C=O); *m*/*z* 483 (M^+, 2%), 423 (23), 394 (2), 121 (100) and 43 (28).

4,6-Dibromo-3-methyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl acetate 25

N-4-Methoxybenzyloxindolone **24** (0.026 g, 0.054 mmol) was dissolved in acetonitrile (0.65 ml) and then water (0.22 ml) was added. The solution was treated with ceric ammonium nitrate (0.118 g, 0.215 mmol), stirred for 3.5 h, then water (10 ml) was added and the mixture extracted with ethyl acetate (2 × 10 ml). The organic extracts were combined, washed with brine and dried ($MgSO_4$). Preadsorption on silica followed by flash silica gel column chromatography afforded the *title compound* **25** (0.016 g; 82%) as colourless needles, mp 155–165 °C (decomp.) (light petroleum–ethyl acetate) (Found: M^+, 362.8929. $C_{11}H_9Br_2NO_3$ requires *M*, 362.8930); ν_{max}(CH_2Cl_2)/cm^{-1} 3420, 1756, 1743, 1612, 1578, 1372, 1172, 1104, 1022, 950 and 841; δ_H(250 MHz; $CDCl_3$) 1.73 (3H, s), 2.13 (3H, s), 7.00 (1H, d, *J* 1.5), 7.31 (1H, d, *J* 1.5) and 8.30 (1H, br s); δ_C(66 MHz; $CDCl_3$) 20.00 (CH_3), 20.23 (CH_3), 77.72 (C), 112.97 (CH), 118.12 (C), 123.55 (C), 126.57 (C), 128.93 (CH), 142.83 (C), 169.39 (C=O) and 176.00 (C=O); *m*/*z* 363 (M^+, 41%), 320 (15), 304 (34), 278 (12), 225 (4) and 43 (100).

Convolutamydine C 3 (alternative method)

The acetate **25** (0.0075 g, 0.0207 mmol) was taken up in ethanol (0.5 ml) and treated with excess aqueous sodium hydroxide (1 M; 5 drops) and the mixture stirred for 3 h. TLC showed clean conversion to the desired product. Thus the mixture was cooled in an ice bath and acidified with dilute hydrochloric acid (4%; 10 drops), saturated with brine and extracted with ethyl acetate (3 × 10 ml). The combined extracts were dried ($NaSO_4$), filtered and concentrated under reduced pressure to give essentially pure (by ^{1}H NMR spectroscopy) convolutamydine C **3**. The solid was preadsorbed on silica and subjected to flash silica column chromatography (2 : 1 light petroleum–ethyl acetate) to yield pure convolutamydine C **3** (0.0061 g, 91%) as a colourless solid; data as given previously.

X-Ray crystallography

Crystal data. Compound **10**: $C_{18}H_{15}Br_2N_3O_3$, $M = 481.14$. Triclinic, $a = 11.176(3)$, $b = 10.440(3)$, $c = 10.007(3)$ Å, $\alpha = 118.18(2)$, $\beta = 68.45(2)$, $\gamma = 100.20(2)°$, $V = 957.2(5)$ Å^3 (by least-squares refinement for 25 centred reflections with $74.09 < 2\theta < 74.78°$, $\lambda = 1.541\,78$ Å, $T = 20$ °C), space group $P\bar{1}$ (no. 2), $Z = 2$, $D_c = 1.70$ g cm^{-3}, clear plate, dimensions 0.15 × 0.15 × 0.21 mm, μ(Cu-Kα) = 47 cm^{-1}, $F(000) = 476$.

Compound **11**: $C_{18}H_{15}Br_2NO_3$, $M = 453.13$. Monoclinic, $a = 11.281(1)$, $b = 13.438(2)$, $c = 12.424(1)$ Å, $\beta = 109.85(1)°$, $V = 1771.5(3)$ Å^3 (by least-squares refinement for 25 centred reflections with $72.67 < 2\theta < 74.87°$, $\lambda = 1.541\,78$ Å, $T = 20$ °C), space group $P2_1/a$ (no. 14), $Z = 4$, $D_c = 1.70$ g cm^{-3}, clear plate, dimensions 0.20 × 0.20 × 0.20 mm, μ(Cu-Kα) = 60 cm^{-1}, $F(000) = 896$.

Compound **13**: $C_{16}H_{13}Br_2NO_2$, $M = 411.09$. Monoclinic, $a = 11.698(2)$, $b = 25.230(4)$, $c = 11.023(2)$ Å, $\beta = 104.19(2)°$, $V = 3154.4(9)$ Å^3 (by least-squares refinement for 25 centred reflections with $45.91 < 2\theta < 56.76°$, $\lambda = 1.541\,78$ Å, $T = 20$ °C), space group Cc (no. 9), $Z = 8$ (two independent molecules), $D_c = 1.73$ g cm^{-3}, clear plate, dimensions 0.03 × 0.10 × 0.24 mm, μ(Cu-Kα) = 66 cm^{-1}, $F(000) = 1616$.

Compound **17**: $C_{19}H_{17}Br_2N_3O_4$, $M = 511.17$. Monoclinic, $a = 18.542(12)$, $b = 9.728(9)$, $c = 23.971(11)$ Å, $\beta = 100.30(5)°$, $V = 4254.1(5)$ Å^3 (by least-squares refinement for 25 centred reflections with $65.00 < 2\theta < 73.56°$, $\lambda = 1.541\,78$ Å, $T = 20$ °C), space group $C2/c$ (no. 15), $Z = 8$, $D_c = 1.60$ g cm^{-3}, clear plate, dimensions 0.18 × 0.18 × 0.20 mm, μ(Cu-Kα) = 51 cm^{-1}, $F(000) = 2032$.

Data collection and processing. Rigaku AFC7S diffractometer, graphite monochromated Cu-Kα radiation, ω–2θ scan method, corrections for Lorentz and polarisation factors, absorption were applied in all cases (DIFABS),[22] as were corrections for linear isotropic crystal decay where noted.

10: 2939 reflections measured ($5.3 \leqslant 2\theta \leqslant 120.4°$, h, $\pm k$, $\pm l$) 2861 unique ($R_{int} = 0.13$, decay of standards 14.4%), giving 2395 observed [$I > 3.00\sigma(I)$] which were used in all further calculations.

11: 2929 reflections measured ($5.3 \leqslant 2\theta \leqslant 120.1°$, h, k, $\pm l$) 2774 unique ($R_{int} = 0.27$), giving 2067 observed [$I > 2.00\sigma(I)$] which were used in all further calculations.

13: 2548 reflections measured ($5.4 \leqslant 2\theta \leqslant 120.2°$, h, k, $\pm l$) 2417 unique ($R_{int} = 0.12$), giving 1402 observed [$I > 3.00\sigma(I)$] which were used in all further calculations.

17: 3498 reflections measured ($5.4 \leqslant 2\theta \leqslant 120.5°$, h, k, $\pm l$) 3373 unique ($R_{int} = 0.03$, decay of standards 10.2%), giving 1677 observed [$I > 3.00\sigma(I)$] which were used in all further calculations.

Structure solution and refinement.[23] The structures were solved by direct methods (**10**, **13** and **17** all non-H atoms) and heavy atom methods (**11**). Full-matrix least-squares refinement on *F*, with all non H-atoms anisotropic except in **17**, where Br(17) was refined in three positions to model disorder. The highest weight (0.5) occupancy position was refined anisotropically and the two minor weight positions (0.25) were refined isotropically. In **13**, solution and refinement were attempted in *C*2/*c*, but proved unsuccessful. Hydrogen atoms were placed in idealised positions. All *R* indices were as defined in ref. 23. All calculations were carried out using the TEXSAN crystallographic software package of Molecular Structure Corporation.[23] Atomic coordinates, bond lengths, angles and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre (CCDC).[12]

10: $R = 0.038$, $R_w = 0.041$. An extinction parameter was included and refined to 2.94×10^{-6}. Maximum peak in the final ΔF map was 0.41 e Å^{-3}.

11: $R = 0.055$, $R_w = 0.054$. An extinction parameter was included and refined to 3.65×10^{-7}. Maximum peak in the final ΔF map was 0.58 e Å^{-3}.

13: $R = 0.030$, $R_w = 0.024$. An extinction parameter was included and refined to 2.98×10^{-7}. Maximum peak in the final ΔF map was 0.19 e Å^{-3}.

17: $R = 0.067$, $R_w = 0.069$. An extinction parameter was included and refined to 8.63×10^{-8}. Maximum peak in the final ΔF map was 0.55 e Å^{-3}.

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