Tetrahedron Vol. 44, No. 10, pp. 2887 to 2892, 1988
Printed in Great Britain.

0040-4020/88 $3.00+.00
Pergamon Press plc

SYNTHESIS OF ARCYRIARUBIN B AND RELATED BISINDOLYLMALEIMIDES[1]

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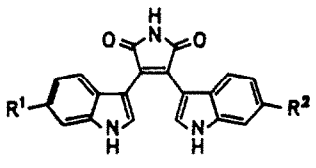
(*Received in Germany* 8 *March* 1988)

Abstract - The reaction of indolyl magnesium bromide with 2,3-dibromo-*N*-methylmaleimide (3) in toluene leads to bisindolylmaleimides 6. In THF a monosubstitution product 5 is obtained which after protection of the indole NH-group with the Boc residue can be used to prepare unsymmetrically substituted bisindolylmaleimides, arcyriarubin B given as an example.

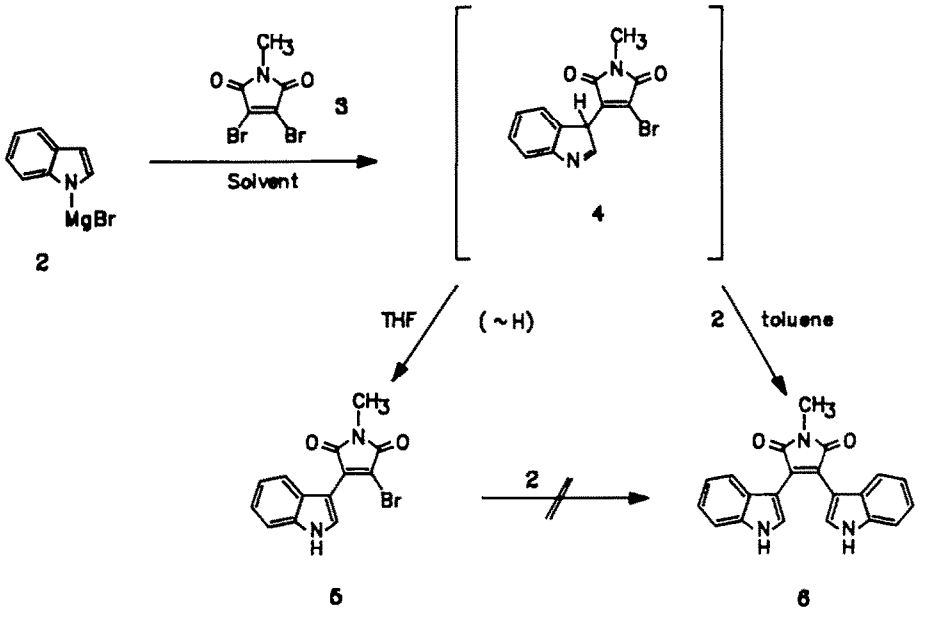
The arcyriarubins A-C[2] (**1a-1c**) represent the simplest members of the bisindolylmaleimides[3], a family of pigments produced by slime moulds (Myxomycetes). They are structurally related to the aglycon of staurosporine[4], SF-2370[5], rebeccamycin[6] and other biologically active metabolites from Streptomycetes.



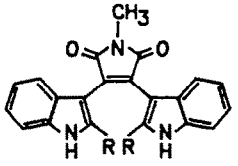
	R^1	R^2
1a	H	H
1b	OH	H
1c	OH	OH

The first synthesis of arcyriarubin A was accomplished by reaction of indolyl magnesium bromide (2) with 2,3-dibromo-*N*-methylmaleimide (3) as the crucial step[2]. This method has since been applied by *Kaniko* et al.[7] and *Weinreb* et al.[8] for the synthesis of rebeccamycin and staurosporine aglycone, respectively. Recently, *Bergman* and co-workers[9] developed a biomimetic synthesis of **1a** *via* oxidative coupling of the dianion derived from β-indolylmethylacetate. In this publication we report details of our arcyriarubin synthesis and its use for the preparation of unsymmetrically substituted derivatives.

The condensation of indolyl-MgBr with **3** in ether/benzene mixtures affords red *N*-methylarcyriarubin (**6**) accompanied by varying amounts of the yellow monosubstitution product **5**, which can be separated easily by column chromatography. The proportions of **5** and **6** are determined by the rates in which the primary adduct **4** is either isomerised to the monoindolyl compound **5** or reacts with a second molecule of indolyl-MgBr to give the bisindolylmaleimide **6**. Because the products **5** and **6** are stronger acids than indole they react with an excess of indolyl-MgBr with salt formation. Therefore, to achieve optimum yields of **5** and **6**, two or four equivalents of **2** have to be applied, respectively.

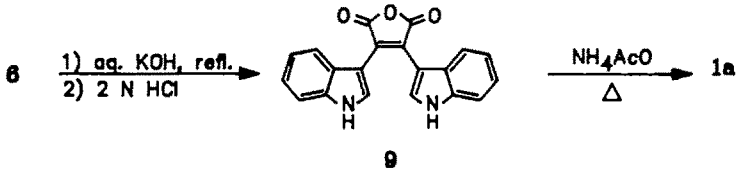


As we have found, the outcome of the reaction is strongly dependent on the solvent. In toluene the reaction gives the bisindolyl compound **6** in 70% yield, whereas in tetrahydrofuran the monosubstitution product **5** is obtained in 74% yield. Obviously, in tetrahydrofuran the isomerisation of **4** to **5** is faster than the reaction of **4** with a second molecule of Grignard reagent. Using the reaction conditions as in the case of **6** the 2,2'-dimethyl- and 2,2'-diphenyl-derivatives **7** and **8** can be obtained. In the later case, however, the yield was only 24% due to the strong sterical interaction of the phenyl substitutents and the low solubility of 2-phenylindole in toluene.

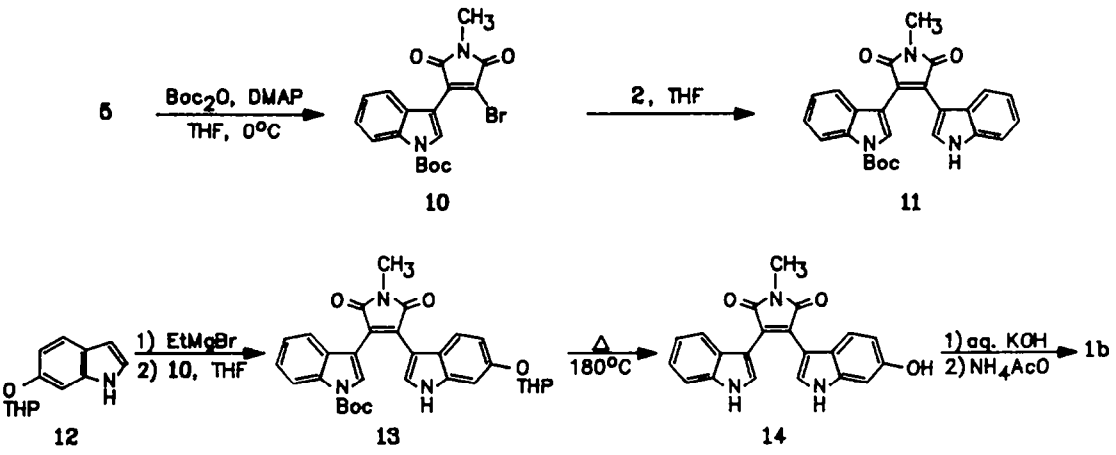


	R
7	CH_3
8	Ph

The conversion of **6** into arcyriarubin A was achieved by alkaline hydrolysis to the cyclic anhydride **9** which on heating with ammonium acetate yielded **1a**. The compound was identical with the natural pigment from *Arcyria denudata*[3].



The monosubstitution product **5** appeared to be suitable for the preparation of unsymmetrically substituted arcyriarubins. However, treatment of **5** with indolyl-MgBr did not lead to the expected product because of salt formation. We therefore converted **5** into its *N-tert*-butyloxycarbonyl derivative **10** by treatment with di-*tert*-butyl dicarbonate in the presence of 4-(dimethylamino)pyridine[10]. **10** reacted smoothly with two equivalents indolyl-MgBr in THF to give the mono-Boc derivative **11** in 85% yield. We then applied the same reaction to the Grignard compound derived from 6-(tetrahydropyranyloxy)indole (**12**) which afforded the coupling product **13** in 89% yield. **12** was prepared from 1-methyl-2-nitro-4-(tetrahydropyranyloxy)benzene according to the method of *Rapoport* and *Feldman*[11].



Because the deprotection of 13 with trifluoroacetic acid gave *N*-methylarcyriarubin B (14) only in about 50% yield, the deprotection was carried out by heating the compound to 180°C[12]. Under these conditions both protecting groups are removed and the free hydroxy compound 14 was obtained in 94% yield. Exchange of the imino group for the methylimino group in the usual way then led to arcyriarubin B (1b) in high overall yield. The synthetic product was in every respect identical with the natural pigment.

Because the arcyriarubins can be oxidatively cyclised to the corresponding arcyriaflavins[2,7,8,9] our method allows the synthesis of unsymmetrical substituted compounds of this type.

EXPERIMENTAL

M.p.s were determined with a Reichert hot-stage microscope and a Büchi melting-point apparatus and are uncorrected. IR spectra were obtained using a Perkin-Elmer 1420 infrared spectrometer. NMR spectra were measured with Varian EM-390, Bruker WH 90 and AC 200 instruments (tetramethylsilane as internal reference). Mass spetra were obtained at 70 ev using an AEI MS 30 or MS 50 spectrometer equipped with a data system. UV spectra were measured with a Varian Cary 17. For column chromatography, Merck silica gel 40 - 63 μm was used. TLC was carried out on TLC aluminum sheets silica gel 60 F_{254}. Elemental analyses were performed at the Institut für Organische Chemie und Biochemie, Universität Bonn. Tetrahydrofuran (THF) and diethyl ether were dried over sodium hydride, toluene by heating over Sicapent (Fa. Merck). The dried solvents were then distilled at atmospheric pressure.

Materials: 2,3-Dibromomaleimide[13] and 2,3-dibromo-*N*-methylmaleimide[14] (3) are known compounds.

2-Bromo-3-(1H-indol-3-yl)-*N*-methylmaleimide (5): A solution of ethylmagnesium bromide in THF (20 ml) was prepared from magnesium turnings (0.72 g, 29.8 mmol) and freshly distilled bromoethane (2.25 ml, 29.8 mmol) under anhydrous conditions. The solution was warmed up to 40°C and indole (3.5 g, 29.8 mmol) in THF (20 ml) was added. After stirring for 30 min at 40°C the mixture was cooled to 20°C and a solution of 2,3-dibromo-*N*-methylmaleimide (4.0 g, 14.9 mmol) in THF (60 ml) was added dropwise over 1 h. The mixture was stirred 2 h at 20°C and hydrolysed by addition of ice-saturated 20% aqueous citric acid. After removal of the THF *in vacuo* the mixture was extracted with ethyl acetate. The combined organic extracts were washed with water and dried ($MgSO_4$). The residue remaining after rotary evaporation of the solvent was recrystallised from methanol. Yield 3.34 g (74%), m.p. 145°C (dec.), R_F 0.63 (trichloromethane/ethyl acetate 6:1), [Found C, 51.13; H, 2.96; N, 9.01; $C_{13}H_9N_2O_2Br$ (305.1) requires C, 51.17; H, 2.97; N, 9.18%]; IR (KBr): ν_{max} 3340, 2920, 1760, 1700, 1600, 1490, 1425, 1380, 1250, 1175, 1130, 1100, 975, 800, 735 cm^{-1}; ^1H NMR (acetone-d_6/DMSO-d_6): δ = 3.03 (3 H, s), 7.00-7.28 (2 H, complex), 7.42-7.57 (1 H, complex), 7.93-8.10 (2 H, complex), 11.58 (1 H, s, br); UV (MeOH): λ_{max} = 431 (lg ϵ = 3.87), 274 (3.95), 250 (4.09), 217 (4.48), 198 nm (4.40).

General procedure for the preparation of symmetrical bisindolylmaleimides 6 - 8

To a solution of ethylmagnesium bromide (50.1 mmol) in THF (20 ml) was added a solution of indole-compound (50.1 mmol) in toluene (60 ml) and warmed up to 45°C for 45 min. Then a solution of 3

(11.2 mmol) in toluene (60 ml) was added dropwise over 1 h, followed by refluxing for 2 h. The reaction mixture was cooled and ice and 20% aqueous citric acid were added. The mixture was extracted with ethyl acetate and the organic extract was dried ($MgSO_4$). The solvent was removed *in vacuo* and the dark red residue was purified by chromatography on silica gel. The eluants used for the chromatography were the same as given for TLC of the individual compounds.

2,3-Bis-(1H-indol-3-yl)-*N*-methylmaleimide (**6**): From **3** and indole, yield 2.66 g (70%), m.p. 278°C (from acetone), R_F 0.35 (trichloromethane/ethyl acetate 6:1), [Found C, 73.73; H, 4.50; N, 12.31; $C_{21}H_{15}N_3O_2$ (341.4) requires C, 73.89; H, 4.43; N, 12.31%]; IR (KBr): ν_{max} 3410, 3290, 1750, 1675, 1610, 1528, 1455, 1420, 1382, 1240, 1181, 1130, 1120, 1102, 1030, 977, 755, 743, 700, 610 cm^{-1}; ^1H NMR (acetone-d_6/DMSO-d_6): δ = 3.07 (3 H, s), 6.56-7.11 (6 H, complex), 7.42 (2 H, td, *J* 8 Hz, 0.9 Hz), 7.79 (2 H, s), 11.71 (2 H, s); ^{13}C NMR (DMSO-d_6): δ = 23.9, 105.8, 111.8, 119.4, 121.1, 121.7, 125.4, 127.2, 129.2, 136.1, 171.9; MS (180°C): m/z = 343 (100%, $MH_2^{+\cdot}$), 342 (23.1, $MH^{+\cdot}$), 341.1148 (97.3, $M^{+\cdot}$, calc. for $C_{21}H_{15}N_3O_2$ 341.1164), 340 (16.1), 258 (74.0), 257 (50.0), 256 (43.5), 255 (41.6), 128 (42.2); UV (MeOH): λ_{max} = 464, 372, 277, 255 nm.

2,3-Bis-(2-methyl-1H-indol-3-yl)-*N*-methylmaleimide (**7**): From **3** and 2-methylindole, yield 3.84 g (93%), m.p. 152°C (from trichloromethane), R_F 0.36 (dichloromethane/acetone 50:1); IR (KBr): ν_{max} 3600, 3060, 2980, 2920, 1755, 1690, 1550, 1460, 1385, 1245, 1210, 745 cm^{-1}; ^1H NMR (DMSO-d_6): δ = 1.98 (6 H, s), 3.00 (3 H, s), 6.61-7.27 (8 H, complex), 8.25 (1 H, s, $CHCl_3$), 11.20 (2 H, s); MS (180°C): m/z = 369.1513 (100%, $M^{+\cdot}$, calc. for $C_{23}H_{19}N_3O_2$ 369.1477), 354 (31.1), 297 (26.2), UV (MeOH): λ_{max} = 465 (lg ϵ = 3.69), 287 (4.05), 278 (4.08), 218 nm (4.56).

2,3-Bis-(2-phenyl-1H-indol-3-yl)-*N*-methylmaleimide (**8**): From **3** and 2-phenylindole in toluene (120 ml) and THF (22.5 ml), yield 1.31 g (24%), m.p. > 330°C (from acetone), R_F 0.58 (trichloromethane/ethyl acetate 20:1), [Found C, 78.17; H, 5.34; N, 7.42; $C_{33}H_{25}N_3O_2$ (493.6) x 1 acetone (551.7), requires C, 78.38; H, 5.30; N, 7.62%]; IR (KBr): ν_{max} 3360, 3050, 1750, 1690, 1530, 1490, 1425, 1380, 1325, 1210, 980, 745, 695 cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.90 (3 H, s), 6.53-7.53 (20 H, complex), 11.5 (2 H, s); UV (EtOH): λ_{max} = 462 (lg ϵ = 3.72), 296 (4.41), 234 (4.63), 204 nm (4.87).

2,3-Bis-(1H-indol-3-yl)-maleic anhydride (**9**): **6** (300 mg, 0.88 mmol) was refluxed for 30 min in 10% aqueous potassium hydroxide (120 ml), cooled and acidified with 2 N HCl. The red precipitate was collected, dried and recrystallised from methanol. Yield 232 mg (80%), m.p. 229°C, [Found C, 73.10; H, 3.72; N, 8.43; $C_{20}H_{12}N_2O_3$ (328.3) requires C, 73.17; H, 3.68; N, 8.50%]; IR (KBr): ν_{max} 3380, 1818, 1750, 1698, 1630, 1610, 1530, 1490, 1458, 1425, 1335, 1245, 1177, 1125, 1010, 930, 818, 742 cm^{-1}; ^1H NMR (acetone-d_6): δ = 6.54-6.71 (2 H, complex), 6.87-7.08 (4 H, complex), 7.40 (2 H, d, *J* 8.4 Hz), 7.86 (2 H, s), 10.93 (2 H, s, br); MS (180°C): m/z = 328.0841 (100%, $M^{+\cdot}$, calc. for $C_{20}H_{12}N_2O_3$ 328.0848), 256 (67.8), 255 (26.8), 228 (7.9), 227 (7.6), 201 (5.8), 200 (5.4).

2,3-Bis-(1H-indol-3-yl)-maleimide (**1a**) (arcyriarubin A): 2,3-Bis-(indol-3-yl)-maleic anhydride (**9**) (200 mg, 0.61 mmol) was heated with ammonium acetate (5 g) at 140°C (bath temperature). After 10 min, the mixture was cooled down, water was added, and the mixture was extracted with ethyl acetate. The extracts were combined, washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was recrystallised from acetone. Yield 160 mg (80%), m.p. 161°C, [Found C, 71.59; H, 5.07; N, 10.78; $C_{20}H_{13}N_3O_2$ (327.4) x 1 acetone (385.4) requires C, 71.68; H, 4.97; N, 10.90%]; IR (KBr): ν_{max} 3370, 3310, 3250, 3060, 1750, 1710, 1630, 1530, 1425, 1342, 1245, 1185, 1135, 1110, 998, 760, 745, 660 cm^{-1}; ^1H NMR (DMSO-d_6): δ = 6.55-7.07 (6 H, complex), 7.38 (2 H, d, *J* 8.1 Hz), 7.74 (2 H, s), 10.80 (1 H, s), 11.59 (2 H, s); MS (180°C): m/z = 327.1008 (100%, $M^{+\cdot}$, calc. for $C_{20}H_{13}N_3O_2$ 327.1008), 326 (30.1), UV (MeOH): λ_{max} = 455 (lg ϵ = 3.79), 368 (3.6), 277 nm (3.9).

2-Bromo-3-[1-(*tert*-butyloxycarbonyl)-1H-indol-3-yl]-*N*-methylmaleimide (**10**): Di-*tert*-butyl dicarbonate (3.44 g, 15.7 mmol) and catalytic amounts of DMAP were added to an ice-cooled solution of **11** (4.0 g, 13.1 mmol) in THF (80 ml) and the mixture was stirred for 40 min at 0°C. After removal of the solvent *in vacuo* the yellow residue was recrystallised from methanol. Yield 4.12 g (78%), m.p. 138°C, [Found C, 53.10; H, 4.35; N, 6.83; $C_{18}H_{17}N_2O_4Br$ (405.3) requires C, 53.35; H, 4.23; N, 6.91%]; IR (KBr): ν_{max} 3170, 2975, 1755, 1700, 1590, 1500, 1450, 1435, 1380, 1370, 1355, 1340, 1260, 1240, 1160, 1148, 1100, 1057, 860, 758, 750 cm^{-1}; ^1H NMR (acetone-d_6): δ = 1.72 (9 H, s), 3.11 (3 H, s), 7.27-7.46 (2 H, complex), 7.85 (1 H, ddd, *J* 7.8, 1.6, 0.8 Hz), 8.17 (1 H, s), 8.22 (1 H, ddd, *J* 8.2, 1.4, 0.8 Hz); ^{13}C NMR ($CDCl_3$): δ = 24.9, 28.1 (3 C), 85.1, 108.7, 115.4, 120.5, 122.5, 123.3, 125.3, 126.9, 129.7, 135.5, 136.6, 148.9, 166.0,

168.7; MS (180°C): m/z = 406 (1.1%), 404 (1.1), 350 (7.6), 348 (7.6), 306 (16.9), 304 (16.9), 57 (100); UV (MeOH): λ_{max} = 390 (lg ϵ = 3.71), 282 (3.86), 248 (4.24), 225 (4.38), 212 (4.41), 198 nm (4.42).

1-Methyl-2-nitro-4-(tetrahydropyranyloxy)benzene[15]: To a solution of 4-methyl-3-nitrophenol (10.0 g 65.2 mmol) and dihydropyran (22 ml, 240 mmol) in ethyl acetate (80 ml) was added a catalytic amount of conc. HCl. After the mixture had been stirred for 72 h at room temperature, 2% aqueous sodium hydroxide (50 ml) was added and the organic layer was twice washed with the same solution and then twice with water. After drying over $MgSO_4$, the solvent was removed *in vacuo* and the residue recrystallised from petroleum ether (40-60°C) at -18°C. Yield 13.69 g (88%), m.p. 58°C, [Found C, 60.57; H, 6.50; N, 5.70; $C_{12}H_{15}NO_4$ (237.3) requires C, 60.75; H, 6.37; N, 5.90], IR (KBr): ν_{max} 3120, 2940, 1565, 1525, 1448, 1355, 1335, 1300, 1275, 1230, 1200, 1180, 1145, 1110, 1030, 1020, 960, 905, 870, 835, 810, 760 cm^{-1}, ^1H NMR ($CDCl_3$): δ = 1.50-1.90 (6 H, complex), 2.5 (3 H, s), 3.50-4.00 (2 H, complex), 5.40 (1 H, t, *J* 2 Hz), 7.20 (2 H, complex), 7.70 (1 H, complex).

6-(Tetrahydropyranyloxy)indole[11] (12): To 1-methyl-2-nitro-4-(tetrahydropyranyloxy)benzene (10.0 g, 42.1 mmol) in dry dimethylformamide (80 ml) were added dimethylformamide dimethyl acetal (20 ml) and pyrrolidine (4 ml). The mixture was heated at 110°C for 14 h under argon, then cooled with ice and diluted with ice-water. Extraction with ether, washing of the combined organic phases with ice-water, drying (Na_2SO_4), and removal of the solvent under reduced pressure yielded a deep red oil. The oil was dissolved in ethyl acetate and hydrogenated at 3.5 atm and 25°C for 3 h using 10% palladium on carbon (1.0 g) as catalyst. The mixture was filtered through a Celite pad and the light brown filtrate was concentrated under reduced pressure. Chromatography of the residue on silica gel using dichloromethane as eluant afforded 12 (4.67 g, 51%). M.p. 84°C (from methanol/water), [Found C, 71.61; H, 7.06; N, 6.51; $C_{13}H_{15}NO_2$ (217.3) requires C, 71.87; H, 6.96; N, 6.45%]; IR (KBr): ν_{max} 3285, 2940, 1622, 1500, 1285, 1250, 1170, 1127, 1097, 1085, 1040, 1030, 1020, 980, 910, 862, 805, 760, 710, 620 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.51-2.13 (6 H, complex), 3.47-3.69 (1 H, complex), 3.84-4.11 (1 H, complex), 5.40 (1 H, t, *J* 2 Hz), 6.47 (1 H, ddd, *J* 3.2, 2, 1 Hz), 6.88 (1 H, dd, *J* 8.6, 2.4 Hz), 7.07 (1 H, "dd", *J* 3.2, 2.4 Hz), 7.13 (1 H, "d", *J* 2 Hz), 7.51 (1 H, d, *J* 8.6 Hz), 8.07 (1 H, s, br); ^{13}C NMR ($CDCl_3$): δ = 19.0, 25.3, 30.6, 62.1, 97.5, 98.6, 102.2, 111.6, 121.0, 123.1, 123.6, 136.4, 153.4; MS (180°C): m/z = 217 (1.4%), 133 (100), 104 (4.9), 86 (12.7), 84 (19.3), 77 (4.2), 49 (26.4); UV (MeOH): λ_{max} = 288 (lg ϵ = 3.74), 268 (3.73), 218 (4.47), 201 nm (4.37).

General procedure for the preparation of unsymmetrical bisindolylmaleimides 11 and 13

To a solution of ethylmagnesium bromide (9.3 mmol) in THF (5 ml) was added a solution of the indole derivative (9.3 mmol) in THF (10 ml). The solution was stirred at 45°C for 1 h after which a solution of 10 (3.7 mmol, 1.5 g) in THF (20 ml) was added dropwise over 1 h, followed by refluxing for an additional hour. The reaction mixture was cooled and hydrolysed by addition of ice-saturated aqueous 20% citric acid. The mixture was extracted with ethyl acetate, the combined organic layers were dried ($MgSO_4$), and the solvent was removed *in vacuo*. Purification of the residue by chromatography on silica gel yielded the pure products. The eluants used were the same as indicated for TLC of the individual compounds.

2-(1-*tert*-Butyloxycarbonyl-1H-indol-3-yl)-3-(1H-indol-3-yl)-*N*-methylmaleimide (11): From 10 and indole, yield 1.39 g (85%), m.p. 200°C, R_F 0.55 (trichloromethane/ethyl acetate 6:1), [Found C, 70.40; H, 5.45; N, 9.35; $C_{26}H_{23}N_3O_4$ (441.5) requires C, 70.74; H, 5.25; N, 9.52%]; IR (KBr): ν_{max} 3360, 2970, 1740, 1690, 1640, 1555, 1420, 1360, 1235, 1150, 1065, 980, 750 cm^{-1}; ^1H NMR (acetone-d_6): δ = 1.62 (9 H, s), 3.09 (3 H, s), 6.57-7.49 (7 H, complex), 7.94-8.19 (3 H, complex), 10.93 (1 H, s); MS (200°C): m/z = 442 (1.7%), 441 (6.0), 385 (7.2), 342 (24.0), 341 (100), 340 (28.0), 324 (17.0), 283 (12.0), 256 (22.0), 255 (27.0); UV (EtOH): λ_{max} = 450 (lg ϵ = 3.95), 369 (3.61), 274 (4.17), 248 (4.37), 215 nm (4.72).

2-(1-*tert*-Butyloxycarbonyl-1H-indol-3-yl)-*N*-methyl-3-(6-tetrahydropyranyloxy-1H-indol-3-yl)-maleimide (13): From 10 and 6-(tetrahydropyranyloxy)indole (12), yield 1.79 g (89%), m.p. 136°C, R_F 0.36 (dichloromethane/acetone 50:1), [Found C, 68.66; H, 6.03; N, 7.60; $C_{31}H_{31}N_3O_6$ (541.6) requires C, 68.75; H, 5.77; N, 7.76%]; IR (KBr): ν_{max} 3370, 2940, 1735, 1700, 1620, 1540, 1450, 1380, 1370, 1355, 1235, 1150, 1110, 1065, 1030, 970, 745 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.68 (9 H, s), 1.50-1.90 (6 H, complex), 3.18 (3 H, s), 3.50-3.60 (1 H, complex), 3.80-3.95 (1 H, complex), 5.10 (1 H, t, *J* 3 Hz), 6.54 (1 H, dd, *J* 8.6, 2.2 Hz), 6.75-6.95 (3 H, complex), 7.00 (1 H, dd, *J* 2.2, 0.4 Hz), 7.15 (1 H, ddd, 8.4, 6.8, 1.6 Hz), 7.65 (1 H, d, *J* 3 Hz), 8.04 (1 H, s), 8.12 (1 H, td, *J* 8.5, 0.8 Hz,), 8.66 (1 H, d, *J* 2 Hz, br); ^{13}C NMR ($CDCl_3$): δ = 18.7, 24.1, 25.1, 28.0 (3 C), 30.3, 61.9, 84.3, 96.9, 98.4, 106.5, 110.9, 112.2, 114.9, 120.3, 121.6, 122.1, 122.5, 123.8, 124.4, 128.1, 128.2, 129.1, 131.6, 135.0, 136.7, 149.2, 153.7, 171.7, 171.9; MS (180°C): m/z =

441.1694 (8.1%, $M^{+\cdot}$, calc. for $C_{26}H_{23}N_3O_4$ 441.1699), 357 (100, $C_{21}H_{15}N_3O_3$), 356 (21.2), 340 (11.4, $C_{21}H_{14}N_3O_2$); UV (EtOH): λ_{max} = 459 (lg ϵ = 3.92), 280 (4.20), 254 (4.36), 219 nm (4.69).

2-(6-Hydroxy-1H-indol-3-yl)-3-(1H-indol-3-yl)-*N*-methylmaleimide (**14**): **13** (530 mg, 0.98 mmol) was heated for 40 min to 180°C (bath temperature). The resulting product was cooled and purified by chromatography on silica gel (eluant: dichloromethane/acetone 5:1) followed by recrystallisation from acetone. Yield 327 mg (94%), m.p. 178°C (from acetone), R_F 0.45 (eluant as indicated above), [Found C, 69.09; H, 5.19; N, 10.04; $C_{21}H_{15}N_3O_3$ (357.4) x 1 acetone (415.4) requires C, 69.39; H, 5.10; N, 10.11%]; IR (KBr): ν_{max} 3390, 2940, 1750, 1690, 1620, 1530, 1440, 1380, 1240, 1155, 830, 740 cm^{-1}; ^1H NMR (acetone-d_6): δ = 3.05 (3 H, s), 6.20 (1 H, "dd", *J* 9, 1.5 HzH), 6.56-7.05 (5 H, complex), 7.37 (1 H, "d", *J* 8.4 Hz), 7.72 (2 H, "dd", *J* 6.9, 2.4 Hz), 7.83 (1 H, s), 10.42 (1 H, s, br), 10.67 (1 H, s, br); MS (180°C): m/z = 357.1113 (100%,$M^{+\cdot}$, calc. for $C_{21}H_{15}N_3O_3$ 357.1113), 356 (24.6), 340 (16.0).

2-(6-Hydroxy-1H-indol-3-yl)-3-(1H-indol-3-yl)-maleimide (**1b**) (arcyriarubin B): **14** (307 mg, 0.86 mmol) was dissolved in 10% aqueous potassium hydroxide (20 ml) at room temperature and the solution was acidified after 5 min with 2 N HCl. The mixture was extracted with ethyl acetate and the extract was evaporated under reduced pressure. The residue was heated with ammonium acetate (5 g) for 30 min at 140°C (bath temperature). The mixture was cooled and after the addition of water extracted with ethyl acetate. The organic layer was washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was chromatographed on silica gel (eluant: dichloromethane/acetone 2:1) and **1b** recrystallised from methanol. Yield 238 mg (81%), m.p. 177°C, R_F 0.56 (eluant as indicated above), [Found C, 67.18; H, 4.82; N, 11.27; $C_{20}H_{13}N_3O_3$ (343.4) x 1 methanol (375.4) requires C, 67.19; H, 4.56; N, 11.19%]; IR (KBr): ν_{max} 3380, 1750, 1700, 1620, 1530, 1450, 1420, 1345, 1240, 1155, 810, 745 cm^{-1}; ^1H NMR (acetone-d_6): δ = 6.23 (1 H, dd, *J* 8.4, 2.1 Hz), 6.67 (2 H, dd, *J* 8.4, 1 Hz), 6.82 (1 H, dd, *J* 2.1, 0.7 Hz), 6.98 (2 H, "dt", *J* 7.7, 1 Hz), 7.39 (1 H, "dt", *J* 7.7, 1 Hz), 7.72 (1 H, "dd", *J* 2.8, 1 Hz), 7.80 (1 H, "dd", *J* = 2.8, 1 Hz), 7.94 (1 H, s, br), 9.67 (1 H, s, br), 10.51 (1 H, s, br), 10.77 (1 H, s, br); ^{13}C NMR (acetone-d_6): δ = 97.6, 107.5, 110.8, 112.3, 120.3, 122.4, 122.7, 122.9, 126.9, 128.3, 128.7, 129.7, 137.2, 138.4, 154.4, 173.4; MS (180°C): m/z = 343.0955 (100%, $M^{+\cdot}$, calc. for $C_{20}H_{13}N_3O_3$ 343.0957), 326 (11.7), UV (MeOH): λ_{max} = 463 (lg ϵ = 3.87), 346 (3.65), 281 (4.01), 201 nm (4.70).

Acknowledgement - We thank the Deutsche Forschungsgemeinschaft for financial support.

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