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BILE PIGMENT STUDIES—III[1,2]

CONTROLLED OXIDATIVE DEGRADATION OF 1,19(21,24H)-BILINDIONES[3,4] (BILITRIENES)

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(Dedicated to Prof. R. B. WOODWARD on the occasion of his 60th birthday)

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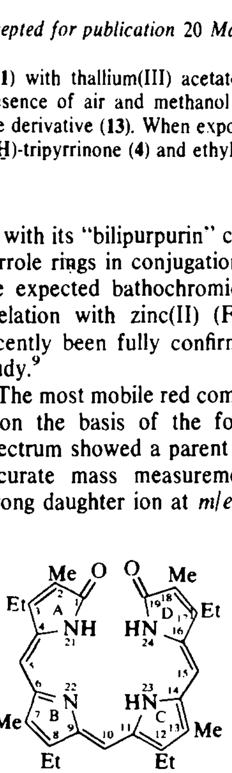
Abstract—Treatment of the model 1,19(21,24H)-bilindione (**1**) with thallium(III) acetate in methanol gives the thallium(III) complex (**11**) which is unstable and in the presence of air and methanol is transformed into the 15,16-dimethoxy complex (**12**), characterised as the metal free derivative (**13**). When exposed to light, solutions of (**12**) are oxidised to afford, after work-up, the 14-formyl-1(15H)-tripyrrinone (**4**) and ethylmethylmaleimide (**17**). A general discussion of mechanistic implications is presented.

In Part I of this Series we described[1] the synthesis of a model bile pigment (**1**). Part II described[2] the formation of 17,18 - dihydro - octaethyl - 1,19(21,24H) - bilindione (**2**) by oxidative ring-opening of *trans*-octaethylchlorin; the bilindione (**2**) has since been shown[5,6] to be a good model for the chromophoric species in both phycocyanin (the antenna pigment of blue-green algae) and the P_r form of phytochrome (the photoreceptor for the regulation of growth in higher plants and some algae). Along with the 17,18-dihydrobilindione (**2**) was also isolated[2] the 16-methoxybilintrione (**3**), produced by further oxidation of **2** at the methine bridge adjacent to the dihydro-ring; since shortening of the chromophore network is a characteristic of the Gmelin reaction, and is evidently important[6] in the $P_r - P_{fr}$ change in phytochrome, we are carrying through an investigation of the controlled oxidation of 1,19(21,24H)-bilindiones (bilitrienes[4]). We have already demonstrated[2] that treatment of the bilindione (**1**) with an excess of lead(IV) acetate resulted in a play of colour similar to that observed in the classical Gmelin reaction,[7] the first reaction of bile pigments to be discovered. It is not surprising[8] that the initial site of oxidation in 1,19(21,24H)-bilindiones is at a terminal methine position; however, so far as we are aware, little has been done on the mechanisms and products from controlled oxidation of such compounds. This paper describes initial studies in this direction.

Addition of thallium(III) acetate to bilindione (**1**) in acetic acid caused the formation of a green solution. This did not persist for any length of time and the colour changed gradually to royal blue. Upon aqueous work-up the solution became red in colour and thick layer chromatography gave starting material (**1**) together with two new red products. The most polar of these was characterised as the 14 - formyl - 1(15H) - tripyrrinone (**4**) on the basis of its elemental analysis, mass spectrum [*m/e* 391 (100%), 362 (48)], and NMR spectrum which showed one aldehydic proton (τ 0.14) and only two methine protons (τ 3.33, 4.13). The infrared spectrum indicated the presence of a formyl group (ν_{max} 1645 cm^{-1}), and the electronic absorption spectrum (Fig. 1), with its "bilipurpurin" character, indicated only three pyrrole rings in conjugation. The spectrum also showed the expected bathochromic shifts upon protonation or chelation with zinc(II) (Fig. 1). The structure **4** has recently been fully confirmed in a single crystal X-ray study.[9]

The most mobile red compound was assigned structure **5** on the basis of the following evidence. The mass spectrum showed a parent ion at *m/e* 556, confirmed by accurate mass measurement as $C_{33}H_{40}N_4O_4$, with a strong daughter ion at *m/e* 390 ($C_{24}H_{28}N_3O_2$; m* at *m/e*



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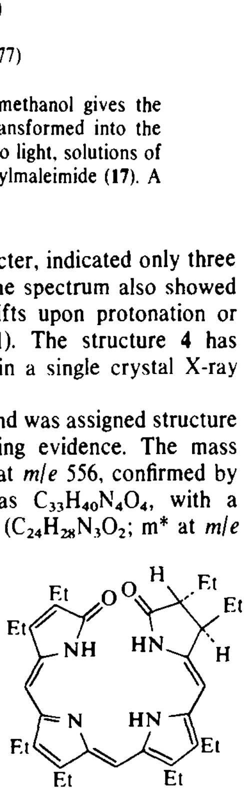

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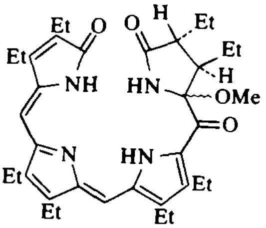

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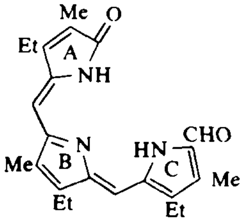

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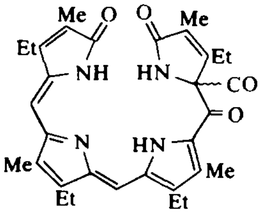

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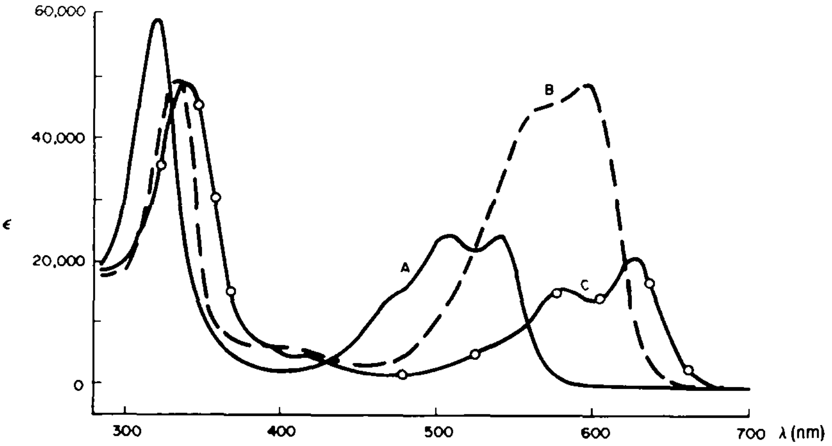
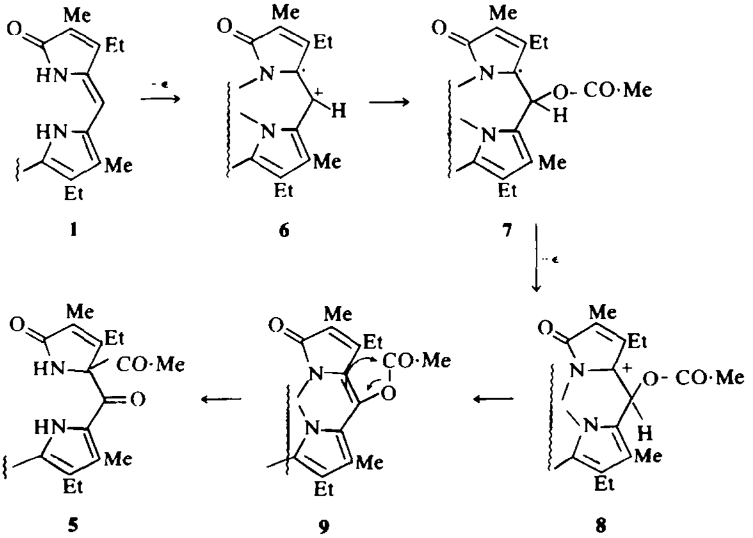


Fig. 1. Electronic absorption spectra of 14-formyl-tripyrrinone (4) in: A, $CHCl_3$; B, $CHCl_3$ + 1%TFA; C, $CHCl_3$ + 1%satd $Zn(OAc)_2$ in MeOH.

273.6). An extra methyl group (CH_3CO) was observed in the NMR spectrum and only two methine protons were evident (τ 3.27, 4.12). In the IR spectrum strong bands at 1727 and 1705 cm^{-1} indicated the presence of extra CO functions, and finally, the electronic absorption spectrum was similar to those of compounds **3** and **4**, suggesting a structure containing three pyrrole rings in conjugation, terminating with a CO function. Though other structures are possible for the new product, on balance we favour **5**. It is possible to speculate on the mechanism for formation of **5**, and this did influence our structural assignment. One electron oxidation of the bilinidione (**1**) [or its thallium(III) complex] would give the cation radical **6** (Scheme 1) which could react with acetate to give **7**. Further one electron oxidation would give the cation **8** which could rearrange via **9** to give the required product **5**. Alternatively, the bilindione (**1**) could suffer initial two electron abstraction to give the corresponding π-dication which might react with acetate and then rearrange to furnish **5**. The overall mechanism has parallels in work described by Lemberg[10] in which 16-nitroso-bilintriones are obtained from treatment of bilindiones with nitric/nitrous acids. The final step (**9**→**5**) is a type of Fries rearrangement.

Addition of a 100% excess of thallium(III) acetate to the bilindione (**1**) resulted in increased yields of the 14-formyltripyrrinone (**4**) at the expense of **5**. Thus, a reproducible route to **4** was developed; a solution of thallium(III) acetate in acetic acid was added to the bilindione (**1**) in the same solvent. After an aqueous work-up, preparative TLC afforded starting material (**1**), a violet pigment, and the 14-formyl-tripyrrinone. The violet pigment, upon re-chromatography, afforded the bilindione (**1**) and 14-formyl-tripyrrinone (**4**), indicating that it was a precursor of the required compound **4**. Owing to its lability, the purple compound has not yet been identified but it is possible that it is an unsymmetrical dimer of the type **10**, produced by reaction of the radical **7** with the cation radical, followed by loss of a proton. Molecular models show that **10** could fragment via a favourable 6-membered transition state to give the bilindione (**1**), tripyrrinone (**4**) and a mono-pyrrolic unit. Further work on the structure of the purple pigment and the mechanism of its decomposition are in hand, but it is

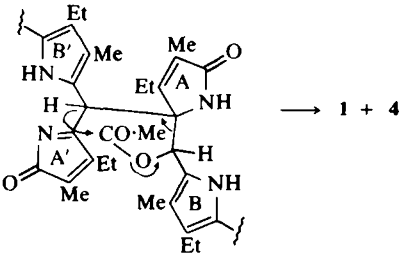


Scheme 1.

worth mentioning in favour of **10** that generically similar bilindione photodimers have been isolated and characterised.[11] Moreover, the chromophore shown in **10** would be expected to give rise to a violet/purple colour [*cf* the 15,16-dimethoxybilindione (**13**), *vide infra*].

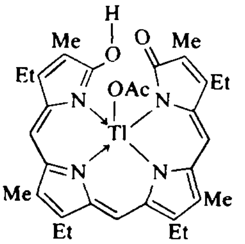
Compounds **4** and **5** were also isolated if the above reactions were carried out using lead(IV) tetra-acetate in place of thallium(III) acetate (Experimental).

Owing to the lability of many of the compounds described above we decided to simplify the work-up procedures by carrying out the reactions in a more volatile solvent, such as methanol. Treatment of the bilindione (**1**) with 1 equiv of thallium(III) acetate in methanol gave rapidly a green solution (Fig. 2) of the thallium(III) complex (**11**). In methanol solution, this complex was unstable, so it was obtained in the solid form by treatment of **1** in methylene chloride with thallium(III) acetate in acetonitrile under nitrogen; gradual addition of n-hexane led to crystallisation. The IR spectrum of this product clearly indicated retention of the acetate ligand ($\nu_{\max}$ 1580 cm^{-1}). When a methanol solution of **11** was stirred in the dark in the presence of air a blue solution (Fig. 2) was produced; this material, though very labile in daylight, was obtained crystalline and its NMR spectrum showed two additional OMe resonances (τ 6.55, 6.76) and only two methine peaks [τ 3.17 ($J_{\text{Tl-H}}$ 25 Hz), 4.12 ($J_{\text{Tl-H}}$ 31 Hz)]. A single NH or OH peak was also observed at τ 0.99. The blue compound was therefore assigned structure **12**, and confirmatory evidence in its favour was obtained by demetallation with acid to give the fully characterised purple 15,16-dimethoxybilindione (**13**). In its NMR spectrum this material showed the expected two OMe's (τ 6.71, 7.04) and two methine resonances (τ 3.26, 4.11) as well as a singlet 15H (τ 5.59). The electronic absorption spectrum (Experimental) was as expected[12] and the mass spectrum with its mass ion at *m/e* 560, showed a fragment ion at *m/e* 406 (100%) due to loss of ring D, together with a metastable ion confirming the cleavage. Final confirmation of the structure has very recently been provided by a single crystal X-ray study[9] which, somewhat surprisingly, shows that the two OMe groups have been added to the same side of the molecule. This may, however, be a result of a subsequent equilibration since



10

(or a solvent adduct in Ring A')



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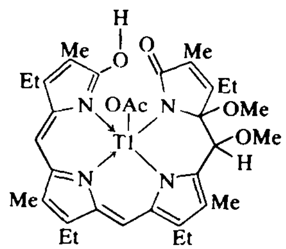

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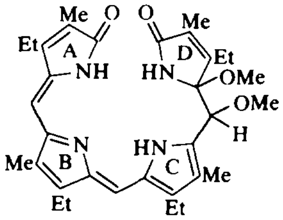

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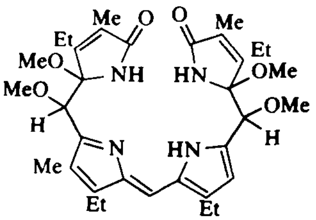

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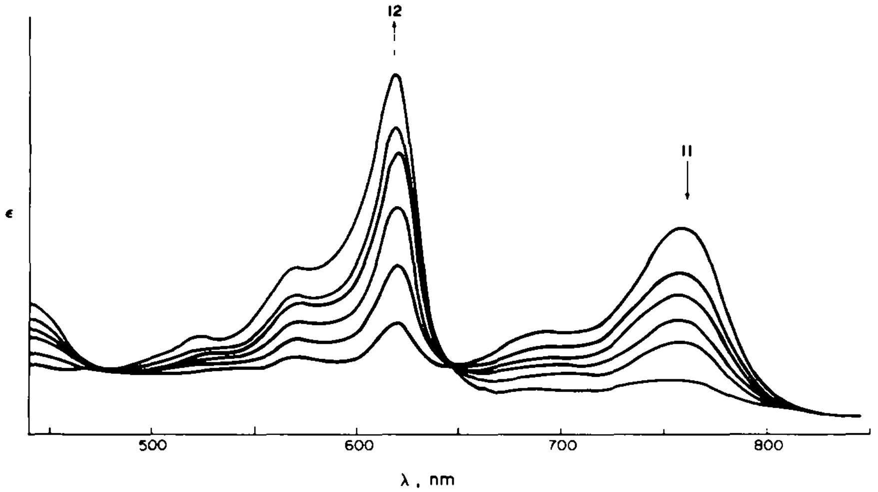


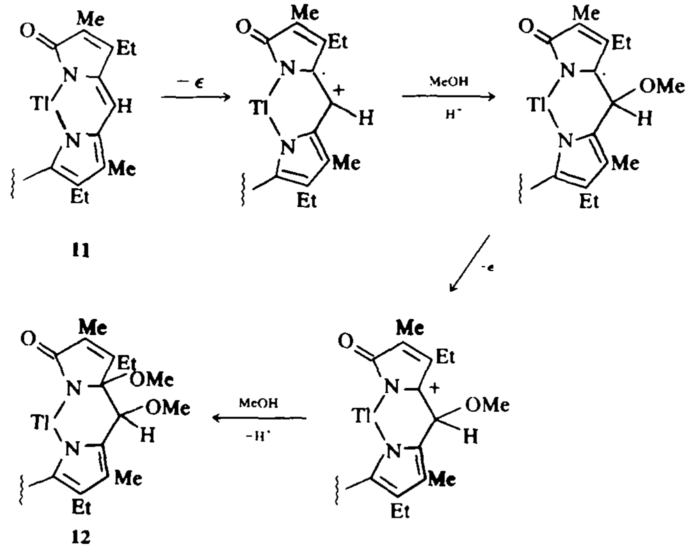
Fig. 2. Electronic absorption spectra showing the transformation of thallium(III) bilindione (11) into thallium(III) dimethoxy-bilindione (12) in MeOH in presence of thallium(III) acetate. Isosbestic points occur at 486 and 646 nm.

we have observed that the 16-OMe group is labile (see also Ref. [12]) in some metal complexes of **13**.

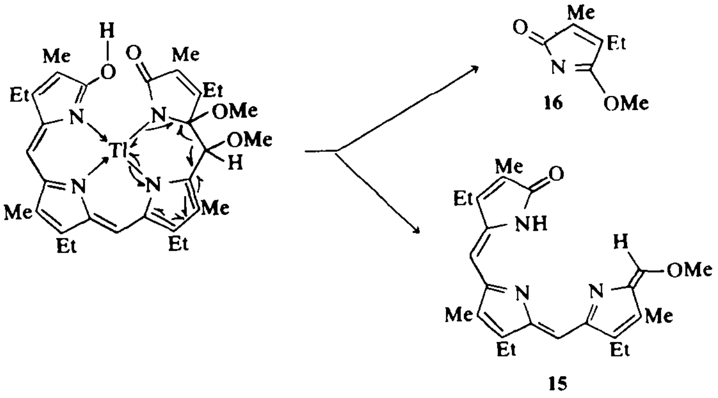
15,16-Dimethoxy-bilindiones of the same type as **13** have been prepared by Siedel[7] and more recently by von Dobeneck,[12] from treatment of bilindiones with bromine in methanol. We interpret the mechanism of this reaction as involving one electron oxidation by bromine to give the cation radical (**6**) which suffers nucleophilic attack by methanol before removal of a second electron and attack by a second molecule of methanol, rather than a mechanism involving addition of Br^+ and MeO^- (produced from reaction between bromine and methanol) and elimination of HBr. In defence of the cation radical mechanism we have demonstrated[13] that anodic oxidation of **1** in methylene chloride–methanol (0.05 M tetra-(n-butyl) ammonium perchlorate) at platinum electrodes gives a good yield of the 15,16 - dimethoxy - bilindione (**13**). At higher potentials the 4,5,15,16 - tetramethoxy - bilindione (**14**) is produced;[13] von Dobeneck has also prepared a similar compound using bromine in methanol.[12]

Formation of **12** is very slow in the absence of oxygen, but the reaction is greatly accelerated by passage of air through the solution of **11**. In view of the fact that thallium(III) reagent is not consumed in the transformation of **11** into **12** we deduce that oxygen is the oxidising agent involved; chelation of **1** with a metal ion would certainly be expected to lower the oxidation potential of the resulting complex. In Scheme 2 we present a plausible mechanism for the formation of **12**.

Treatment of the metal-free 15,16-dimethoxybilindione (**13**) with thallium(III) acetate in methanol regenerated the blue solution of the thallium(III) complex **12** (Fig. 2). Compounds with similar electronic absorption spectra were obtained when **13** was treated with zinc(II) or copper(II) acetates; a slight bathochromic shift was observed with the diamagnetic nickel(II) complex, from **13** and its NMR spectrum indicated that one of the OMe's was absent. Work on the characterisation and chemistry of these metal complexes will be reported in a future paper. Unlike the free base **13** and the zinc(II), copper(II) and nickel(II) complexes from it, the thallium(III) complex **12** in methanol solution was unstable towards light, a red solution being formed. Aqueous work-up and preparative TLC gave ethylmethylmaleimide **17** (identified by TLC comparison[14] with an authentic sample), de-metallated dimethoxybilindione (**13**), and the 14-formyl-tripyrrinone (**4**) described earlier. We interpret the mechanism of this novel photocleavage as shown in Scheme 3. A large amount of work has already been carried out on the photochemistry of thallium(III) compounds,[15] and formation of thal-



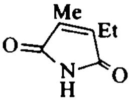
Scheme 2.



Scheme 3.

lium(I) and a diradical, as shown in Scheme 4, is not unexpected. Under the conditions of the work-up the two vinyl ethers (**15** and **16**) would be transformed into the formyl-tripyrrinone (**4**) and ethylmethylmaleimide (**17**) respectively.

In conclusion, the work described above shows that oxidation of bilindiones (bilitrienes) produces transformations at the terminal 5(15)-methine bridges, and that these reactions occur with great facility. Cleavage of the terminal ring at the 4-5 (15-16) bond is also shown to be a common transformation; Scheer *et al.*[16] have recently observed basically similar cleavage reactions.



17

EXPERIMENTAL

M.ps were measured on a microscopic hot stage apparatus. TLC monitoring was performed using thin layers of silica on glass plates. Preparative TLC was carried out on 20 × 20 cm plates using Merck GF 254 silica (1.5 mm thickness). Visible absorption spectra (solns in $CHCl_3$) were measured on a Unicam SP 800 spectrophotometer, and proton NMR spectra were determined (in $CDCl_3$ soln with TMS as internal standard) with a Varian XL-100 or Perkin-Elmer R-34 instrument. Mass spectra (direct insertion probe, 70 eV, 50 μA, source temp. *ca.* 200°) were measured using an AEI MS 12 spectrometer.

Compound **1**[4] was prepared as previously described[1] from t-butyl 4 - ethyl - 3,5 - dimethylpyrrole - 2 - carboxylate.

Reaction of bilindione (1) *with thallium*(III) *acetate in* HOAc. Bilindione **1** (102 mg) in HOAc (35 ml) was treated with thallium(III) acetate (84 mg; 1.1 equiv) and stirred vigorously during 30 min. The mixture was poured into H_2O (1 l.) and neutralised with aqueous ammonia. The precipitated pigments were extracted into $CHCl_3$ which was dried (Na_2SO_4) and evaporated to dryness. Preparative TLC (elution with 20% ethyl acetate in toluene) separated three major bands; the most mobile of these was extracted from the silica, and after evaporation of the solvent gave the 16 - *acetyl* - 1,15,19 - *bilintrione* **5** (10.6 mg; 9.3%), m.p. 187–188° crystallised from ether/n-hexane. (Found: C, 71.00; H, 7.02; N, 9.78. $C_{33}H_{40}N_4O_4$ requires: C, 71.18; H, 7.24; N, 10.07%), τ, 3.27, 4.12 (each 1 H, s methine-H); 7.2–7.6 (8 H, m $C\underline{H}_2CH_3$); 7.51, 7.67, 7.92, 8.08, 8.12 (each 3 H, s β-Me and COMe); 8.3–8.95 (12 H, m $CH_2C\underline{H}_3$). MS, *m/e* 556 (17%), 391 (40), 390 (100), and 362 (6); m* 273.6 (556 → 390) and 336.0 (390 → 362). ν_{max}(KBr) 1668, 1705 and 1727 cm^{-1}. λ_{max} 324 (ϵ 55,000), 476 sh (14,600), 505 (25,500) and 542 nm (26,000); in $CHCl_3$ + 1% TFA, 334 (ϵ 52,000), 566 (48,000) and 590 sh nm (46,500).

The band of medium polarity was removed from the plate and the silica was extracted. Evaporation gave a red residue which was crystallized from Et_2O/n-hexane to give 20.5 mg (25%) of the 14-*formyltripyrrinone* (**4**), m.p.181–183°. (Found: C, 73.40; H, 7.59; N, 10.94. $C_{24}H_{29}N_3O_2$ requires: C, 73.62; H, 7.47; N, 10.74%), τ, 0.14 (1 H, s CHO); 2.22 (2 H, br s NH); 3.33, 4.13 (each 1 H, s methine-H); 7.37, 7.44, 7.60 (each 2 H, q $C\underline{H}_2CH_3$); 7.68, 7.95, 8.02 (each 3H, s β-Me); 8.65–9.00 (9 H, m $CH_2C\underline{H}_3$). MS, *m/e* 391 (100%), 376 (79), 362 (48), 348 (22), 347 (17), 334 (30), 285 (61), 257 (96), and 241 (70); m* 335.2 (391 → 362), and 308.2 (362 → 334). ν_{max}(KBr), 1645 (CHO), 1712, and 1700 cm^{-1}. λ_{max} 543 (ϵ 25,800), 510 (26,300), 486 inf (18,200), and 322 nm (60,100); in $CHCl_3$ + 1% TFA, 596 (ϵ 51,600), 559 sh (46,400), and 330 nm (49,000); in $CHCl_3$ + 1% saturated $Zn(OAc)_2$ in MeOH. 630 (ϵ 22,300), 582 (17,000), 538 sh (7900), and 337 nm (49,000). See Fig. 1 for electronic spectra of **4**.

The most polar band was shown to be the starting material **1**, (41 mg, 40%) crystallised from CH_2Cl_2/MeOH.

Repetition of the above experiment using 2.1 equiv of thallium(III) acetate gave 5.9 mg (5.2%) of **5** and 25.0 mg (30.5%) of **4**. Using 3.1 equiv of thallium(III) acetate the yield of **5** was negligible, and 25.0 mg (30.5%) of **4** was again obtained.

Addition of thallium(III) acetate (80 mg; 1.1 equiv) in HOAc (5 ml) to bilindione **1** (100 mg) in HOAc(25 ml), followed by an aqueous work-up gave pigments which were chromatographed on thick layer plates (elution with 3% MeOH in CH_2Cl_2). The products separated into three bands, none of which contained **5**. The most mobile band was shown, by comparison with material obtained above, to be **4**; the next most polar band contained **1**, and the band of lowest polarity (which was violet in colour) was shown by analytical TLC to disproportionate into pigments **1** and **4**. Repeated preparative TLC (elution with 3% MeOH in CH_2Cl_2) eventually transformed all of the violet material into **1** and **4**, the yield of 14 - formyl - tripyrrinone being 35% (or about 70% based on consumed starting material). A possible structure for the violet compound is suggested in the text.

Reaction of bilindione (1) *with lead* (IV) *tetra-acetate in* HOAc

(i) *Formation of* 16 - *acetyl* - 3,8,12,17 - *tetraethyl* - 2,7,13,18 - *tetramethyl*-1,15,19(21,24H)-*bilintrione* (**5**). The bilindione (200 mg) was stirred in HOAc (20 ml) while being treated in small portions with lead(IV) tetra-acetate (178 mg; 1 equiv). After stirring during 3 days the mixture was neutralised with Na_2CO_3 aq and the precipitated pigments were extracted with CH_2Cl_2. The purple residue was separated on preparative TLC plates (elution with benzene/ether, 8:3) to give two major bands. The most mobile (extracted with 5% MeOH in CH_2Cl_2) was shown, by comparison with authentic material prepared above, to contain **5** (35 mg; 16%). The most polar (blue) band was shown to contain starting material (**1**).

(ii) *Formation of* 3,8,12 - *triethyl* - 14 - *formyl* - 2,7,13 - *trimethyl* - 1(15H) - *tripyrrinone* (**4**). The bilindione **1** (100 mg) was stirred vigorously in HOAc (35 ml) during portionwise addition, over 30 min, of lead(IV) tetra-acetate (89 mg; 1 equiv). After stirring for 1 hr further, the mixture was poured into H_2O (1 l.) and neutralised with strong ammonia (1:1 of 880 ammonia and H_2O). The precipitated pigments were extracted with $CHCl_3$ which was dried (Na_2SO_4) and evaporated to give a red-purple residue. This material was separated on preparative TLC plates (elution with 3% MeOH in CH_2Cl_2) to give two bands. The most polar of these was shown to contain starting bilindione, but the mobile fraction was extracted from the silica (using 5% MeOH in CH_2Cl_2) and evaporated to give the 14 - formyl - tripyrrinone (30 mg; 38%) after crystallisation from ether/n-hexane. This material was identical with the same compound described earlier.

Reactions in MeOH

3,8,12,17 - *Tetraethyl* - 15 - *hydro* - 15,16 - *dimethoxy* - 2,7,13,18 - *tetramethyl* - 1,19(21,24$\underline{H}$) - *bilindione* (**13**). The bilindione **1** (100 mg) in MeOH (25 ml) was stirred during addition of thallium(III) acetate (79 mg; 1.05 equiv) in MeOH (8 ml), and then during a further 16 hr. The mixture was evaporated and the residue was taken up in CH_2Cl_2 (50 ml) containing TFA (1 ml) and then washed with H_2O (3 × 200 ml) before filtration of the organic phase through a bed of Kieselgel G. The filtrate was evaporated and the residue was applied to preparative TLC plates in CH_2Cl_2. The plates were developed in 3% MeOH/CH_2Cl_2 and gave three main bands. The most mobile of these contained **4** (2 mg; 3%), identical with the material described earlier. The band of medium polarity was extracted from the silica with 5% MeOH/CH_2Cl_2 and after evaporation of the extracts and crystallisation from CH_2Cl_2/n-hexane gave the 15,16- - *dimethoxybilindione* **13** (48 mg; 54%), m.p. 168–170°. (Found: C, 70.39; H, 7.91; N, 10.01. $C_{33}H_{44}N_4O_4$ requires: C, 70.68; H, 7.91; N, 9.99%), τ, 3.26 (1 H, s 10-H); 3.89 (1 H, br s NH); 4.11 (1 H, s 5-H); 5.59 (1 H, s 15-H); 6.71, 7.04 (each 3 H, s OMe); 7.3–7.6 (6 H, m), 7.7–7.9 (2 H, q) $C\underline{H}_2CH_3$; 7.94, 7.96, 8.07 8.16 (each 3 H, s β-Me); 8.7–9.1 (12 H, m $C\underline{H}_2CH_3$). MS (*cf.* Ref. [12]), *m/e* 560 (1%), 528 (5), 498 (10), 406 (100). ν_{max}(KBr), 3260, 1710, and 1585 cm^{-1}. λ_{max} 325 (ϵ 41,000), 522 sh (24,000), 552 nm (30,600); in $CHCl_3$ + 1%TFA, 328 (35,500), 550 (54,000).

The most polar band was green in colour and after extraction from the silica gave the thallium(III) complex (**11**) of the bilindione (30 mg; 20%), m.p. > 300°. Owing to partial demetallation during removal from the silica, a satisfactory analysis could not be obtained. However, demetallation with TFA followed by an aqueous work-up gave a quantitative yield of **1**, which could be re-converted into the thallium(III) complex as follows: **1** (45 mg) in CH_2Cl_2 (15 ml) under N_2 was treated with thallium(III) acetate (30 mg; 1 equiv) in acetonitrile (5 ml) and stirred for 10 min. n-Hexane was then added dropwise, keeping the whole system under N_2, until crystallisation occurred. The product was filtered off (40 mg; 58%) and shown to be identical, by TLC, with the material described above. The thallium(III) complex was unstable in soln (possibly due to radical formation) and a satisfactory NMR was not obtained. The combustion analysis was consistently low on carbon, (Found: C, 49.42; H, 5.00; N, 7.23. $C_{33}H_{39}N_4O_4Tl$ requires: C, 52.14; H, 5.17; N, 7.37%). λ_{max} (in MeOH), 762 (ϵ 42,400), 692 (19,700), and 383 nm (50,000). On the 400 mg (of **1**) scale, isolated products were as follows: **4** (70 mg; 22%); **13** (196 mg; 44%); **11** (135 mg; 22%). Occasionally, 90% yields of **13** were obtained; Fig. 2 shows the transformation of **11** into **12** to be quantitative at spectroscopic dilution.

3,8,12,17 - *Tetraethyl* - 15 - *hydro* - 15,16 - *dimethoxy* - 2,7,13,18 - *tetramethyl* - 1,19(21,24$\underline{H}$) - *bilindione thallium*(III) *complex* (**12**). Bilindione **1** (50 mg) in MeOH (25 ml) was treated, in the dark, with thallium(III) acetate (100 mg) in MeOH (5 ml) and left to stir for 1 hr. The blue mixture was filtered through a bed of silicagel, and then evaporated to dryness. Crystallisation from CH_2Cl_2/n-hexane gave the *product* (48 mg; 60%), m.p. > 300°. τ, 0.99 (1 H, s NH or OH); 3.17 (1 H, d J 25 Hz, 10-H); 4.12 (1 H, d J 31 Hz, 5-H); 5.53 (1 H, d J 9 Hz); 6.55, 6.76 (each 3 H, s OMe); 7.0–7.8 (8 H, m $C\underline{H}_2CH_3$); 7.9–8.2 (12 H, m Me); 8.4–9.0 (12 H, m $CH_2C\underline{H}_3$). λ_{max} (in MeOH), 620 (ϵ 55,000), 572 (22,500) and 333 nm (42,000). The product was unstable in the daylight (see text); demetallation with TFA followed by an aqueous work-up gave an almost quantitative yield of **13**, which when treated in the dark with thallium(III) acetate in MeOH regenerated **12** in 74% yield, using the same work-up as described above. If a soln of the thallium(III) complex (50 mg) in MeOH (50 ml) was stirred in daylight during 8 hr the soln became red in colour; work-up and preparative TLC (elution with 5% MeOH/CH_2Cl_2) gave two major bands. The most mobile pigment was the 14-formyltripyrrinone and the most polar was the 15,16 - dimethoxy-bilindione; proportions of these two products were variable and depended upon the reaction time and the intensity of light used. An aliquot of the reaction mixture was subjected to analytical TLC using the conditions described by Rüdiger[14] for development and detection of maleimides; a spot with the same R_f as authentic **17** was observed.

3,8,12,17 - *Tetraethyl* - 2,7,13,18 - *tetramethyl* - 1,19 - (21,24$\underline{H}$) - *bilindione nickel*(II) *complex*. Bilindione **1** (100 mg) in CH_2Cl_2 (15 ml) was treated with a soln of nickel(II) acetate (400 mg) in MeOH (10 ml) under reflex for 1 hr (mixture blue → green). The mixture was evaporated to dryness and the residue was taken up in CH_2Cl_2 and chromatographed on a column of Fluka neutral alumina (100 g, Brockmann Grade III; elution with CH_2Cl_2). The green eluates were evaporated to dryness and the residue was crystallised from CH_2Cl_2/n-hexane to give the *nickel complex* (50 mg; 45%), m.p. > 300°. (Found: C, 67.13; H, 6.48; N, 10.20. $C_{31}H_{36}N_4NiO_2$ requires: C, 67.04; H, 6.53; N, 10.09%). The compound appeared to be paramagnetic since no peaks were observed when attempts were made to measure its NMR spectrum. MS, *m/e* (^{58}Ni) 554 (100%).

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