SYNTHESES WITH 5-DIBROMOMETHYL- AND 5-FORMYL-PYRROMETHENES[1]

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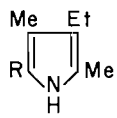
ABSTRACT

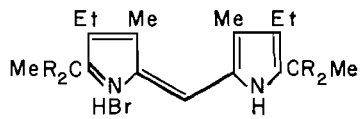
With many 5,5′-dimethyl- and 5-bromo-5′-methyl-pyrromethenes the sequence $CH_3 \rightarrow CH_2Br \rightarrow CH_2OMe$ had been possible. With two such pyrromethenes the following new sequences have been developed: (1) $CH_3 \rightarrow CHBr_2 \rightarrow CH(OMe)_2$ or CHO (cf. III*e* and IV*e*), (2) $CH(OMe)_2$, CHO, or $CH_2OMe \rightarrow Br$ (cf. III*f* and IV*f*), (3) (dimethoxy-methyl-)pyrromethene → formyl-dipyrrylmethane (cf. IX and VII). These provide new intermediates for new porphyrin syntheses and alternative or improved routes to established intermediates.

INTRODUCTION

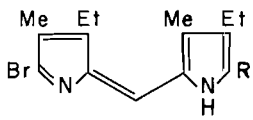
The pyrrole I*a* is readily converted to III*a* by bromine in acetic acid, or to IV*a* by formic and hydrobromic acids, and its analogues behave likewise. The halogenation of



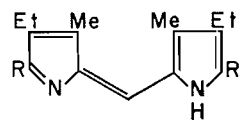
I a ; R = H
I b ; R = COOEt



II a ; $R_2 = H_2$
II b ; $R_2 = HBr$
II c ; $R_2 = Br_2$



III



IV

(a) R = CH_3
(b) R = CH_2Br
(c) R = $CHBr_2$
(d) R = CHO
(e) R = $CH(OMe)_2$
(f) R = Br
(g) R = CH_2OMe

such 5,5′-dimethyl- and 5-bromo-5′-methyl-pyrromethenes to the corresponding bromomethyl derivatives is quite general when the other substituents are purely alkyl, and a 5-carbethoxy-5′-methyl-pyrromethene behaved likewise (1). Further, the bromomethyl-derivatives are readily converted into methoxymethyl-pyrromethenes. When, however, there are other halogen substituents or when the alkyl substituents are carboxylated, the halogenation frequently fails; therefore dihalomethyl- or trihalomethyl-pyrromethenes were unknown. In particular, we have not been able to halogenate 5-bromo-5′-methyl-pyrromethenes with acetic acid and propionic acid residues in the 3(3′) and 4(4′) positions to obtain desired intermediates.

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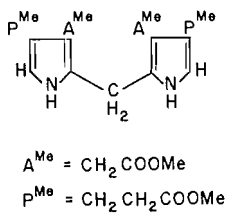
Hans Fischer had reported that an excess of undiluted bromine converted II*a* to a product containing five atoms of bromine but no perbromide (2, 3*a*). It seemed reasonable to assume that his product was not II*b* as provisionally formulated, but II*c*, and that this method of bromination might lead to hitherto unaccessible halogenated pyrromethenes.

This halogenation was also interesting in another connection. Pyrromethenes with acyl groups (formyl or keto) in the 3(3′) and 4(4′) positions were known (3*b*) but 5-acyl-pyrromethenes were only known as their 5′-hydroxy-derivatives (3*c*). This would be expected from the low reactivity of 2-free-5-acyl pyrroles and the exceptional reactivity of 5-free-5′-hydroxy-pyrromethenes. Further, we have failed to convert 5-bromomethyl- to 5-formyl-pyrromethenes in trials with 2-nitropropane, dimethyl–sulfoxide, or selenium dioxide. Recently, however, 4,3′,5′-trimethyl-3,4′-diacetyl-5-formyl-pyrromethene has been obtained from the corresponding 5-free-dipyrrylmethane by reaction with zinc cyanide and hydrogen chloride (4).

We first studied the bromination of the hydrobromides of III*b* and IV*b*. These were presumably favorable cases because the hydrobromides of III*a* and IV*a* are readily halogenated (to those of III*b* and IV*b*) by bromine in acetic acid. An excess of undiluted bromine at room temperature converted the hydrobromides of III*b* and IV*b* into those of III*c* and IV*c*. Later these were obtained directly under more vigorous conditions from the hydrobromides of III*a* and IV*a* but in equally good yield.

Treatment with methanol followed by alkali converted III*c* and IV*c* into the acetals III*e* and IV*e*. Here the 5-bromo group in the acetal III*e* remained intact, whereas that in 5-*bromo*-4,4′-dimethyl-5′-*carbethoxy*-pyrromethene-3,3′-dipropionic acid hydrobromide is reportedly converted into hydroxyl by cold methanolic hydrogen chloride (5). Although the aldehyde III*d* was obtained from III*c* by treatment with sodium acetate, this reaction failed with IV*c*. Possibly 5,5′-diformyl-, like 5,5′-dicarbethoxy-pyrromethenes (6), exist as carbinols rather than as pyrromethene bases, and unprotected 5,5′-diacyl-pyrromethenes may be generally less stable than the corresponding dipyrrylmethanes.

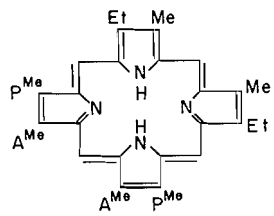
In the same way as 5,5′-diformyl-dipyrrylmethanes condense with 5,5′-free-dipyrrylmethanes at room temperature to form porphyrins (7), the pyrromethene IV*e* condensed with V to form the porphyrin VI (see also below). The yield was low (17%), perhaps because of the rigidity of an open-chain intermediate, and this new method has no obvious advantage over that using analogues of IV*b* (7) at 100°.



A^{Me} = CH_2COOMe

P^{Me} = CH_2CH_2COOMe

V



VI

Bromine in acetic acid converted the aldehyde III*d* or its acetal III*e* into the new unsymmetrical 5,5′-dibromo-pyrromethene III*f*. The two previously known unsymmetrical 5,5′-dibromo-pyromethenes had been obtained from dipyrrylmethanes (8, 9). Bromine also converted IV*e* into the symmetrical IV*f*. The full sequence now permits the conversion of a 5-methyl- to a 5-bromo-pyrromethene. A more convenient equivalent was later found

in the bromination of the methoxymethyl derivatives, III*g* and IV*g* also being converted to III*f* and IV*f*.

Fischer's methods permitted a single pyrrole (e.g. I*a* or I*b*) to be converted unambiguously into pyrromethenes leading to porphyrins (e.g. etioporphyrins) of types 1 and 4. The synthesis of pyrromethenes leading to type 2 and 3 porphyrins required, in addition, the isomeric pyrrole (e.g. 2,3-dimethyl-4-ethyl-pyrrole) (10), which might be much less accessible. However, when extended by the above sequence replacing methyl by bromine, the same methods would also give types 2 and 3 porphyrins from the one pyrrole (Chart I).

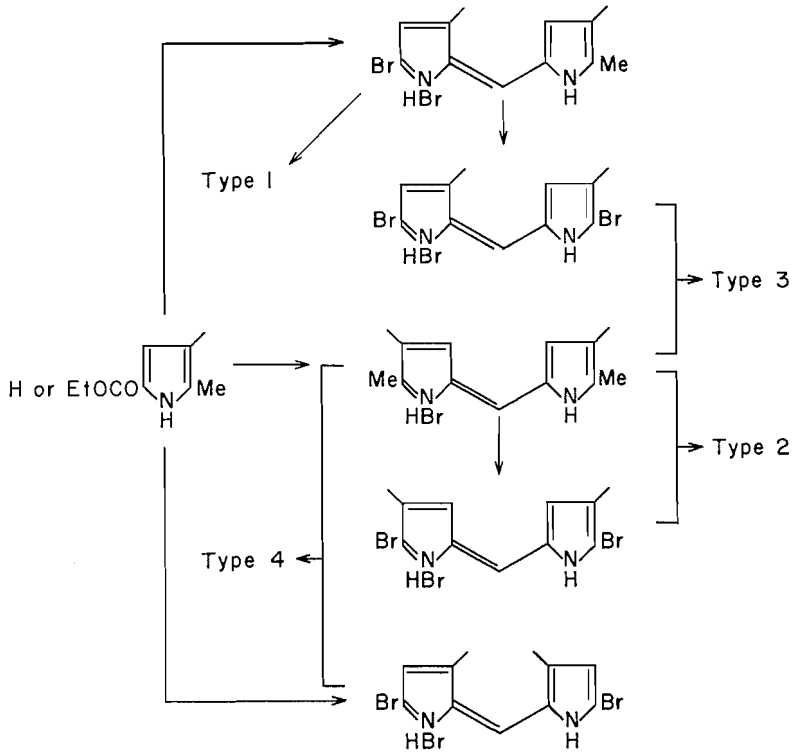
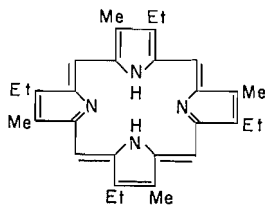
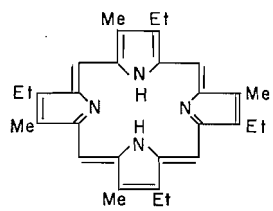


CHART I.

To illustrate this, etioporphyrin 3 (XI) was prepared from III*f* and IV*b*, which required a total of 8 steps compared to the 16 of Fischer's unmodified methods. There are less direct methods by which four isomeric porphyrins could be obtained unambiguously from one pyrrole: one pyrrole could be converted into its isomer (11), or types 2 (7, 12) and 3 (12) porphyrins could be obtained by unrelated methods.



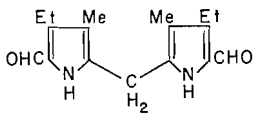
X



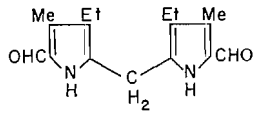
XI

The pyrromethene acetal IV*e* was reduced to the diformyl-dipyrrylmethane VII. This sequence, too, complements an established one, which proceeds over inherently less stable dipyrrylmethanes to convert, for example, *Ib* into VIII (13), the symmetrical isomer of VII. The condensation of VII with V led to the same porphyrin (VI) that was obtained from IV*e* and V (above), but the yield was better (36%). This porphyrin was further identified by degradation to the known mesoporphyrin 4.

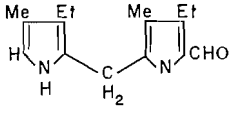
This synthesis of porphyrins from a 5,5′-free- and a 5,5′-diformyl-dipyrrylmethane, like that from a 5,5′-dibromo- and a 5,5′-dimethyl-pyrromethene, requires that one component be symmetrically substituted to avoid an inseparable mixture of two isomers (7). It is thus not applicable to type 1 porphyrins. It suggests, however, a second porphyrin synthesis from two identical or different 5-free-5′-formyl-dipyrrylmethanes which, like the synthesis from two 5-bromo-5′-methyl-pyrromethenes (3*d*, 14), has different symmetry requirements. Accordingly III*d* was reduced but the unstable product, evidently IX, has not been isolated. However, this product did condense to etioporphyrin 1 (X, 44%), which was identified by comparison with authentic material.



VII



VIII



IX

It will be noted that the methoxymethyl- and formyl-pyrromethenes are for some purposes equivalent. However, we have assumed that the reduction of the latter would lead to more stable dipyrrylmethanes. A 5-carboxy-5′-formyl-dipyrrylmethane is reported elsewhere (15).

The nuclear magnetic resonance spectra of all the pyrromethenes and of the diformyl-dipyrrylmethane (Table I) were unambiguous and confirmed the structures assigned.

EXPERIMENTAL

5-Bromo-4,3′-dimethyl-3,4′-di-ethyl-5′-bromomethyl-pyrromethene Hydrobromide (Hydrobromide of IIIb) (3e)

The corresponding 5′-methyl-pyrromethene hydrobromide (III*a*, 2 g (3*f*, 16)) was dissolved in 50 ml of hot acetic acid, bromine (1.2 g) in acetic acid (15 ml) was added, and the solution was heated for 4 h on a steam bath. After the mixture had stood overnight at 20°, the crystalline product was separated out and treated under reflux with acetone for 10 min. The product which separated from the cooled solution was recrystallized from chloroform–hexane as red prismatic crystals (1.8 g, 75%) that decomposed above 250°.

5-Bromo-4,3′-dimethyl-3,4′-di-ethyl-5′-methoxymethyl-pyrromethene (IIIg) (3e)

The corresponding 5′-bromomethyl-pyrromethene hydrobromide (III*b*, 500 mg, prepared as above or, if prepared according to Fischer (3*e*), recrystallized twice from chloroform–hexane) was dissolved in 10 ml of methanol and boiled under reflux for 2 min. Then the solution was cooled and neutralized with 10% sodium hydroxide. The product was recrystallized from methanol as orange–brown needles (290 mg, 79%), m.p. 92–94°.

Unless precautions are taken to ensure that the starting material contains no 5′-methyl-pyrromethene (III*a*), the product has the lower melting point (84°) that has been previously recorded (3*e*).

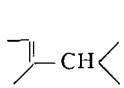
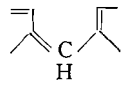
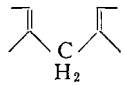
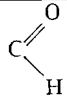
5-Bromo-4,3′-dimethyl-3,4′-di-ethyl-5′-(dibromomethyl)-pyrromethene Hydrobromide (Hydrobromide of IIIc)

(*a*) The corresponding 5′-bromomethyl-pyrromethene hydrobromide (III*b* (3*e*), 500 mg, twice recrystallized from chloroform–petrol) in 3 ml of bromine was stirred at 20° for 1 h. Excess bromine was then completely removed *in vacuo* and the residue was treated under reflux for 30 min with 10 ml of acetone to dissociate any perbromide. After it had cooled the crystalline product was separated off and recrystallized from chloroform as red-brown prisms (450 mg, 77%) that decomposed above 200°, λ_{max} mμ (ϵ) in chloroform: 504 (112 000). The analytical sample was recrystallized once.

Calcd. for $C_{16}H_{20}N_2Br_4$: C, 34.31; H, 3.60; N, 5.00; Br, 57.09. Found: C, 34.49; H, 3.78; N, 5.24; Br, 56.89.

TABLE I

Chemical shifts of pyrromethenes and a dipyrrylmethane (p.p.m., τ-scale)

		—CH_2CH_3	—CH_2CH_3	—OCH_3						Solvent
III*a*	7.97; 7.66	8.82; 8.93	7.33; 7.44				2.95			$CDCl_3$
HBr	7.34									
III*b*	7.92; 7.63	8.77; 8.80	7.19; 7.35		5.05		2.73			$CDCl_3$
HBr										
III*c*	7.59; 7.84	8.70; 8.70	7.15; 7.15			2.82	2.58			$CDCl_3$ + CF_3COOH
HBr										
III*d*	7.85; 8.05	8.86; 8.82	7.46; 7.27				3.37		0.25	$CDCl_3$
III*e*	7.79; 8.01	8.90; 8.85	7.49; 7.41	6.60; 6.60		4.37	3.17			$CDCl_3$
III*f*	7.55; 7.96	8.81; 8.79	7.28; 7.30				2.75			$CDCl_3$
HBr										
III*g*	7.83; 8.03	8.91; 8.86	7.56; 7.44	6.62	5.53		3.25			$CDCl_3$
IV*a*	7.69; 7.69	8.92; 8.92	7.56; 7.56				2.83			$CDCl_3$
HBr	7.33; 7.33									
IV*b*	7.55; 7.55	8.56; 8.56	7.36; 7.36		5.17; 5.17		2.42			$CDCl_3$ + CF_3COOH
HBr										
IV*c*	7.54; 7.54	8.69; 8.69	7.12; 7.12			2.83	2.32			$CDCl_3$ + CF_3COOH
HBr										
IV*e*	7.82; 7.82	8.90; 8.90	7.50; 7.50	6.54; 6.54 6.54; 6.54		4.53; 4.53	3.15			$CDCl_3$
IV*f*	7.81; 7.81	8.87; 8.87	7.55; 7.55				3.27			$CDCl_3$
IV*g*	7.83; 7.83	8.81; 8.81	7.54; 7.54	6.57; 6.57	5.52; 5.52		3.23			$CDCl_3$
VII	7.93; 7.93	8.80; 8.80	7.77; 7.77					6.04	0.44; 0.44	$CDCl_3$

(*b*) The corresponding 5′-methyl-pyrromethene hydrobromide (III*a* (3*f*), 300 mg) and 3 ml of bromine were held under reflux for 1 h on a steam bath, then left at 20° for 1 h. The product was isolated as above. It formed red-brown prisms from chloroform (310 mg, 74%) that decomposed above 200°.

Its identity with the product of (*a*) above was established from their conversion to the same 5′-formyl-pyrromethene (see below).

5-Bromo-4,3′-dimethyl-3,4′-di-ethyl-5′-formyl-pyrromethene (IIId)

The corresponding 5′-(dibromo-methyl)-pyrromethene hydrobromide (III*c*, 560 mg, prepared by method (*a*) above) in 20 ml of chloroform, and saturated aqueous sodium acetate (10 ml, warmed to 60°) were stirred together for 1 h. The chloroform layer was washed with water, dried, and the solvent removed *in vacuo*. The residue was recrystallized from methanol as brown prisms (300 mg, 89%), m.p. 135–138° (dec.). Recrystallized for analysis, it melted at 138–140° (dec.), λ_{max} mμ (ϵ) in 95% ethanol: 270 (9 800); 434 (30 500).

Calcd. for $C_{16}H_{19}N_2OBr$: C, 57.32; H, 5.71; N, 8.36; Br, 23.84. Found: C, 57.16; H, 5.67; N, 8.21; Br, 24.00.

When the starting material was prepared by method (*b*) above, the product (84%) had m.p. 136–139° (dec.), and mixed melting point unchanged.

5-Bromo-4,3′-dimethyl-3,4′-di-ethyl-5′-formyl-pyrromethene Dimethyl Acetal (IIIe)

The corresponding 5′-(dibromo-methyl)-pyrromethene hydrobromide III*c* (200 mg) was treated under reflux with 2.5 ml of methanol for 5 min, cooled, and neutralized with 5% sodium hydroxide. The product, which crystallized after the container was scratched and refrigerated, was recrystallized from methanol as brown needles (100 mg, 84%), m.p. 99–100°, 100–101° after recrystallization for analysis. λ_{max} mμ (ϵ) in 95% ethanol: 271 (7 600); 432 (25 000).

Calcd. for $C_{18}H_{25}N_2O_2Br$: C, 56.70; H, 6.61; N, 7.35; Br, 20.95. Found: C, 56.72; H, 6.45; N, 7.52; Br, 21.08.

5,5′-Dibromo-4,3′-dimethyl-3,4′-di-ethyl-pyrromethene Hydrobromide (Hydrobromide of IIIf)

(*a*) Bromine (0.1 ml in 1 ml of acetic acid) was added to a solution of the aldehyde III*d* (100 mg) in 2 ml of acetic acid. The solution was stirred at 20° for 30 min; then the solvent was removed *in vacuo*. The residue was treated under reflux for 10 min with 5 ml of acetone. The crystalline product (100 mg, 71%) separated from the refrigerated solution. For analysis, it was recrystallized from chloroform–ether as red prisms that decomposed above 140°, λ_{max} mμ (ϵ) in 95% ethanol: 230 (22 000); 452 (76 000).

Calcd. for $C_{15}H_{19}N_2Br_3$: C, 38.57; H, 4.10; N, 6.00; Br, 51.33. Found: C, 38.73; H, 4.22; N, 5.89; Br, 51.08.

(*b*) The acetal III*e* was treated as in (*a*) above to give the product (69%) as red prisms that decomposed above 140°. Found: Br, 51.20.

(*c*) The 5′-methoxymethyl-pyrromethene (III*g*, m.p. 92–94°, 200 mg) dissolved in 4 ml of acetic acid was treated with bromine (0.2 ml) in acetic acid (4 ml). The mixture was heated for 2 h on a steam bath, the product was isolated as in (*a*) above, and washed with ether before it was recrystallized from chloroform–ether. It formed red prisms (160 mg, 61%) that decomposed above 140°.

The nuclear magnetic resonance spectra of the product obtained as under (*a*), (*b*), and (*c*) were identical.

Etioporphyrin 1 (X)

(*a*) The aldehyde III*d* (50 mg) was hydrogenated (6 h, 20°, 1 atmosphere) in 10 ml of 95% ethanol containing 0.2 ml of triethylamine, over 20 mg of palladium black (uptake 6.9 ml, calcd. for $2H_2$:7.2 ml). The catalyst was separated by decantation and the solvent was evaporated *in vacuo* from the initially pale yellow solution. The residue, evidently IX, was dissolved in 10 ml of acetic acid containing 0.2 ml of hydroiodic acid (56%, decolorized with hypophosphorous acid). After 1 h, 1 g of anhydrous sodium acetate in 15 ml of acetic acid was added, and air was passed through for 24 h while the mixture was kept in the dark. The crude product was precipitated with 25 ml of water, separated out, treated under reflux with 5 ml of methanol, separated out again, and crystallized from chloroform–methanol (yield: 15.5 mg, 44%). For analysis it was recrystallized as well-formed red prisms that decomposed above 380° (17) (evacuated capillary), λ_{max} mμ (relative density) in chloroform: 497 (1); 533 (0.73); 567 (0.49); 620 (0.36).

Calcd. for $C_{32}H_{38}N_4$: C, 80.29; H, 8.00. Found: C, 80.50; H, 8.28.

Both the aldehyde III*d* and its acetal III*e* were reduced as above to nearly colorless solutions (dark red in the absence of triethylamine) but they darkened rapidly, and the product has not been isolated.

(*b*) Authentic etioporphyrin 1 was prepared from the mixed hydrobromides (3*e*) of III*a* and III*b* in formic acid (3 *g*), in the form of red prisms (from chloroform–methanol) that decomposed above 380°.

X-ray powder photographs indicated the identity of the two specimens and showed that both existed in two forms. The analytical specimen obtained as under (*a*) was the first form, which was converted by one recrystallization into a mixture of the first and second forms. The specimen obtained as under (*b*) was the second form, and it was converted by one recrystallization into the first form. The X-ray powder photographs of the first forms were identical.

Etioporphyrin 3 (XI)

The hydrobromides of the pyrromethenes III*f* (40 mg) and IV*b* (40 mg) were heated for 1 h with 400 mg of succinic acid, and the product was isolated as in an analogous synthesis (3 *h*). From chloroform–methanol it separated as elongated prisms (4.8 mg, 12%) that decomposed above 355° (17) (evacuated capillary), λ_{max} mμ (relative density) in chloroform: 500 (1); 535 (0.72); 569 (0.49); 623 (0.36).

5,5′-Di-(dibromo-methyl)-3,3′-dimethyl-4,4′-di-ethyl-pyrromethene Hydrobromide (Hydrobromide of IVc)

(*a*) The corresponding 5,5′-di-(bromomethyl)-pyrromethene hydrobromide (IV*b* (16, 18), 1.5 g) was stirred for 1 h at 20° with 10 ml of bromine, the bromine was then removed *in vacuo*, and the residue was boiled under reflux for 30 min with 20 ml of acetone. The crystals were separated from the cooled mixture, washed with cold acetone, and recrystallized from chloroform as orange–red needles (1.2 g, 61%) that decomposed above 200°, λ_{max} mμ (ϵ) in chloroform: 252 (12 100); 519 (126 000). The analytical sample was recrystallized once.

Calcd. for $C_{17}H_{21}N_2Br_5$: C, 31.27; H, 3.25; N, 4.29; Br, 61.19. Found: C, 31.42; H, 3.37; N, 4.27; Br, 61.02.

(*b*) The 5,5′-dimethyl-pyrromethene hydrobromide (IV*a*, 300 mg) was brominated on a steam bath, and the product was isolated exactly as in the direct conversion of III*a* to III*c* (see above). The product crystallized from chloroform as orange-red needles (340 mg, 59%) that decomposed above 200°.

The identity of the products as obtained under (*a*) and (*b*) was established by the identity of their nuclear magnetic resonance spectra and by their conversion to the same acetal (see below).

5,5′-Diformyl-3,3′-dimethyl-4,4′-di-ethyl-pyrromethene Tetramethyl Acetal (IVe)

The corresponding 5,5′-di-(dibromo-methyl)-pyrromethene hydrobromide (IV*c*, 1 g, prepared by method (*a*) above) was boiled under reflux for 5 min in 10 ml of methanol. The solution was neutralized with 5% sodium hydroxide and refrigerated. The crystalline product was separated out and recrystallized from methanol as brown needles (450 mg, 77%), m.p. 63–64°. The analytical sample had been recrystallized as orange–brown needles, m.p. 65°, λ_{max} mμ (ϵ) in chloroform: 443 (24 700).

Calcd. for $C_{21}H_{32}N_2O_4$: C, 66.99; H, 8.57; N, 7.44. Found: C, 66.83; H, 8.45; N, 7.61.

When the starting material was prepared by method (*b*), above, the product (71%) had a melting point of 64–65°, and mixed melting point unchanged.

When IV*c* in chloroform was stirred with aqueous sodium acetate, the black product showed no bands in its visible spectrum.

5,5′-Dibromo-3,3′-dimethyl-4,4′-di-ethyl-pyrromethene Hydrobromide (Hydrobromide of IVf)

(*a*) Bromine (0.2 ml) in 2 ml of acetic acid was added to the acetal IV*e* (100 mg) dissolved in 2 ml of acetic acid. The solution was stirred for 30 min, then concentrated to one-half volume *in vacuo*. The crystalline product which separated out was treated under reflux with 2 ml of acetone for 5 min. The product (80 mg, 65%) was separated as red crystals that decomposed at 200°. The analytical sample was recrystallized from chloroform–ether as red prisms that decomposed at 200° (lit. (3*i*): dec. at 200°, as prepared from 2,3-dimethyl-4-ethyl-5-carbethoxy-pyrrole, the isomer of I*b*), λ_{max} mμ (ϵ) in 95% ethanol: 271 (20 600); 443 (79 000).

Calcd. for $C_{15}H_{19}N_2Br_3$: C, 38.57; H, 4.10; N, 6.00; Br, 51.33. Found: C, 38.54; H, 3.94; N, 5.88; Br, 51.21.

(*b*) The 5,5′-di-(methoxymethyl)-pyrromethene (IV*g* (3*j*), free base, m.p. 85°, 200 mg) dissolved in 4 ml of acetic acid was treated with 0.2 ml of bromine in 2 ml of acetic acid, the solution was heated in a steam bath for 2 h, then concentrated *in vacuo* to one-half volume. The crystals which separated were treated by reflux with 3 ml of acetone for 5 min. When the solution cooled, red prisms separated (160 mg, 54%) that decomposed above 200°. The product was recrystallized from chloroform–ether.

The identity of the products obtained as under (*a*) and (*b*) was established by comparing their free bases: 100 mg of the hydrobromides were dissolved in 2 ml of ethanol, the solutions were neutralized with 5% sodium hydroxide, and then refrigerated. The products which separated were recrystallized from 95% ethanol as orange needles (60 mg, 72%) m.p. 176°, mixed melting point unchanged (lit. (3*i*): 175–176°). Their nuclear magnetic resonance spectra were identical.

5,5′-Diformyl-3,3′-dimethyl-4,4′-di-ethyl-dipyrrylmethane (VII)

The acetal IV*e* (250 mg) was hydrogenated (20°, 1 atmosphere) in 15 ml of 95% ethanol over 70 mg of palladium black for 16 h (uptake 15.6 ml, calcd. for 1 mole:16.1 ml). After the catalyst was removed the solvent was evaporated *in vacuo*, and the crystalline residue was recrystallized from tetrahydrofuran-*n*-hexane as pale yellow prisms (170 mg, 89%), m.p. 245–247°. Recrystallization gave the colorless analytical sample, m.p. 250°, λ_{max} mμ (ϵ) in chloroform 301 (29 100); 320 (27 800).

Calcd. for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.42; H, 7.91; N, 9.95.

The hydrogenation (16 h) was prolonged to allow complete hydrolysis of the acetal; otherwise the product contained methoxy.

2,3-Dimethyl-1,4-di-ethyl-porphin-6,7-di-acetic acid-5,8-dipropionic acid Tetramethyl Ester VI

(*a*) The diformyl-dipyrrylmethane VII (14 mg) and dipyrrylmethane-3,3′-di-acetic acid-4,4′-dipropionic acid tetramethyl ester (V (7), 23 mg) were separately dissolved in warm acetic acid. The cooled solutions were combined, diluted to 10 ml with acetic acid, and 5 ml of acetic acid containing 0.2 ml of 56% hydroiodic acid was added. After 1 h, 1 g of anhydrous sodium acetate in 15 ml of acetic acid was put in, and the solution was aerated in the dark for 24 h. The precipitate was separated out, washed with acetic acid then with methanol, and left overnight in 5% methanolic hydrogen chloride. The solution was mixed with chloroform and ice water. The chloroform layer was well washed with water, dried with sodium sulfate, then passed through Grade IV alumina, which was eluted with 5% methanol in chloroform. The eluate was filtered and concentrated, and the chloroform finally displaced with methanol. The product (13 mg, 36%) separated as curly hairlike needles, m.p. 219–220°. For analysis it was recrystallized as above from chloroform–methanol as

red-brown hairlike needles, m.p. 220–222°, λ_{max} mμ (relative density) in chloroform: 501 (1); 537.5 (0.66); 572 (0.46); 626.5 (0.30).

Calcd. for $C_{40}H_{46}N_4O_8$: C, 67.59; H, 6.52; N, 7.88. Found: C, 67.78; H, 6.70; N, 7.71.

It was tested for scrambled products (etioporphyrins) by shaking an ethereal solution of the porphyrin-free acid with aqueous sodium hydroxide; the ether layer then showed no visible absorption. Further, the diformyldipyrrylmethane (VII) under the conditions of the synthesis but in the absence of V gave no porphyrin.

(*b*) The diformyl-pyrromethene tetramethyl acetal (IV*e*) was condensed with V as in (*a*) above to give a product (17%) with m.p. 218–220°, from chloroform–methanol. It was recrystallized as red-brown hairlike needles, m.p. 220–222°, which was unchanged when it was mixed with the product of (*a*) above. The X-ray powder photographs of the products of (*a*) and (*b*) were identical.

The porphyrin as obtained by method (*a*) above was degraded at 190° to mesoporphyrin 4, (VI, Me for A^{Me}) by the method used to degrade uroporphyrin 2 to coproporphyrin 2 (7). The methyl ester of the product (69%) crystallized from chloroform–methanol as prisms, m.p. 235° (lit. (3*k*): 233°; 238° corr.), λ_{max} mμ (relative density) in chloroform: 502 (1); 536.5 (0.72); 569 (0.48); 623 (0.35).

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