The Preparation and Properties of Thiophen Analogues of Porphyrins and Related Systems: the Linear Tetrathiophens

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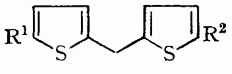
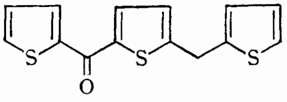
ALTHOUGH the porphyrin system has been intensively investigated for many years, very little has been reported on the hetero-isosteres. Thus the so-called oxaquaterenes (furan analogues of the porphyrinogen system) have been prepared[1] and certain porphyrins with hetero-bridge atoms[2] are known. However, no systems are known incorporating the thiophen ring. We now report syntheses of the first thiophen analogues of the linear tetrapyrroles.

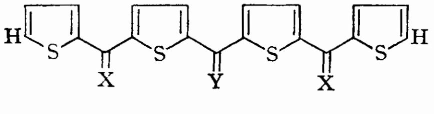


(I)

(a) $R^1=R^2=H$
(b) $R^1=R^2=Ac$
(c) $R^1=Li$, $R^2=H$
(d) $R^1=R^2=Li$



(II)



(III)

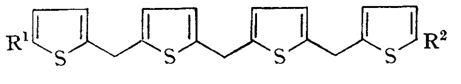
(a) $X=O$; $Y=H_2$
(b) $X=H_2$; $Y=H,OH$
(c) $X=H,OH$; $Y=H_2$
(d) $X=Y=O$
(e) $X=O$; $Y=H,Na$
(f) $X=O$; $Y=Na_2$
(g) $X=O$; $Y=H,Me$
(h) $X=O$; $Y=Me_2$
(i) $X=O$; $Y=-[CH_2]_4-$

Acylation of 2,2′-dithienylmethane (Ia) has been reported to give only moderate yields of ketones, thus with acetic anhydride and iodine, the diacetyl compound (Ib) was obtained[3] while the use of 2-thenoyl chloride and stannic chloride gave a low yield of the monothenoyl derivative (II).[4] The latter ketone (II) is obtained in high yield when only small quantities of stannic chloride are used, while use of polyphosphoric acid (PPA), 2-thenoic acid (2 moles) and 2,2′-dithienylmethane (Ia) (1 mole) at 50° for 2·5 hr. gives the tetrathiophen (IIIa) in 90—95% yield, m.p. 122—123°. This ketone is readily reduced in high yield to the parent system (IVa) by the Huang-Minlon method or with lithium aluminium hydride–aluminium chloride.[5] Use of 2-bromo-5-thenoic acid instead of 2-thenoic acid in the above PPA-catalysed reaction gave the corresponding ketone (IIIa; H = Br), which was reduced with some loss of bromine by lithium aluminium hydride–aluminium chloride.

Another route to the tetrathiophen system lay in the addition of mono- and di-lithio-derivatives (Ic and Id) of 2,2′-dithienylmethane to suitable carbonyl compounds. The metalation of 2,2′-diethienylmethane was found to be very dependent on temperature. Thus only mono-metalation occurred at temperatures below $-10°$ while above 0° dimetalation was observed.[6] By treating the monolithio-derivative (Ic) with ethyl formate the carbinol (IIIb) was obtained; while the reaction of the dilithio-compound with thiophen-2-aldehyde gave the diol (IIIc), m.p. 104—106°. Both of these alcohols decomposed on standing and attempts to protect the hydroxyl groups with benzyl or tosyl halides were without success.

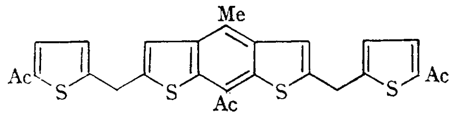
The diketone (IIIa) readily formed a deep turquoise sodio-derivative even with aqueous ethanolic sodium hydroxide, which with oxygen was rapidly converted to the triketone (IIId),[3] m.p. 258—260°. By use of sodium hydride in dry tetrahydrofuran under nitrogen, both mono- and di-sodio-derivatives (IIIe and IIIf) were formed, which by treatment with alkyl halides lead to mono- or di-alkylated derivatives (IIIg, IIIh, and IIIi).

Attempted metalation of the tetrathiophen (IVa) with butyl-lithium in ether under a variety of conditions led consistently to a mixture of mono- and di-lithio-derivatives (IVb and IVc) together with tarry products, which were converted to the mono- and di-carboxylic esters (IVd and IVe) with carbon dioxide followed by diazomethane. Furthermore, attempts to formylate the compound by the Vilsmeier–Haack procedure or to acetylate it with acetic anhydride and a catalyst (phosphoric acid or stannic chloride) were without success. However, use of PPA and acetic acid at 100° gave a product, m.p. 218–220°, which from analytical and spectral data was assigned the structure (V), formed by an Elbs-type cyclisation of an acetylated tetrathiophen. Bromination of the compound (IVa) with bromine under a variety of conditions was accompanied by tar formation to give mainly the dibrominated product (IVf) together with some monobromo-compound (IVg). However, iodination with iodine and mercuric oxide led to high yields of the pure di-iodo-derivative (IVh). This compound was readily converted to the dicarboxylic ester (IVe) by way of the lithio-derivative (IVc).



(IV)

(a) $R^1=R^2=H$
(b) $R^1=H$, R^2Li
(c) $R^1=R^2=Li$
(d) $R^1=H$, $R^2=CO_2Me$
(e) $R^1=R^2=CO_2Me$
(f) $R^1=R^2=Br$
(g) $R^1=H$, $R^2=Br$
(h) $R^1=R^2=I$



(V)

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[5] J. Broome, B. R. Brown, A. Roberts, and A. M. S. White, *J. Chem. Soc.*, 1960, 1406.

[6] Ya. L. Goldfarb and M. L. Kirmalova [*J. Gen. Chem.* (*U.S.S.R.*), 1956, **26**, 3797] reported the formation of a mixture of mono- and di-acids from the carboxylation of metalated 2,2′-dithienylmethane with butyl-lithium (1:2 moles) in ether at −5° to 0°.