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Synthesis of [2₄](2,5)Thiophenophanetetraene or [24]Annulene Tetrasulfide

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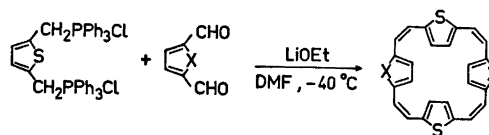
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We have recently developed a convenient method for the preparation of various [2₄]-cyclophanes and related compounds from aromatic dialdehydes and bistrisphenylphosphonium salts of bis(halomethyl)arenes by Wittig reactions at low temperatures.^{1,2} Such cyclophanes are interesting starting materials for the synthesis of circulenes,³ helicenes,⁴ and annulenes. [2₄]Paracyclophanetetraene and the thiophene and furan derivatives contain a conjugated perimeter with 24 electrons and could formally be regarded as derivatives of [24]annulene. Although reasonably planar,⁵ [2₄]paracyclophanetetraene does not show a paramagnetic ring current, i.e. it is not paratropic.⁶ Among the bridged [18]annulenes, [18]annulene trioxide or [2₃]furanophanetriene has

been characterized as aromatic.⁸ In the corresponding sulfur compound, the three sulfur atoms are too large to be accommodated in a planar conformation. Thus the compound cannot sustain a diamagnetic ring current over the perimeter,⁷ nor can [2₃]paracyclophanetriene.⁹


The heterobridged [24]annulenes have been studied less. Two isomers of [2₄]furanophanetetraene or [24]annulene tetroxide have been reported, both being similar to [24]annulene.¹⁰ Some uncertainty in the structural assignment (*cis/trans* isomerism) has made conclusions less firm.

We now report the synthesis of [2₄](2,5)-thiophenophanetetraene, **1**, from 2,5-thiophenedicarbaldehyde and the bistrisphenylphosphonium salt of 2,5-bis(chloromethyl)thiophene. An unstable [2](2,5)furan[2](2,5)thiopheno[2](2,5)furan[2](2,5)thiophenophanetetraene, **2**, was also prepared analogously from 2,5-furandicarbaldehyde (Scheme 1). The symmetrical structure of the compounds follows from their simple ¹H NMR spectra. Both cyclophanes were isolated as the all-*cis* isomers. [2₄](2,5)-Thiophenophanetetraene, **1**, shows a simple mass spectrum with the singly and doubly charged molecular ions as the major peaks. The absorption maximum (354 nm) is shifted 51 nm towards longer wavelengths as compared with [2₄]paracyclophanetetraene.¹ An attempted photocyclization of [2₄](2,5)thiophenophanetetraene in the presence of air and traces of iodine to give tetrathia[8]circulene was not successful, nor was the photocyclization of [2₄]paracyclophanetetraene,³ [2](2,5)-thiopheno[2]paracyclo[2](2,5)thiopheno[2]paracyclophanetetraene or [2](2,5)furan[2]paracyclo[2](2,5)furan[2]paracyclophanetetraene.²



Scheme 1. 1 X=S, 2 X=O.

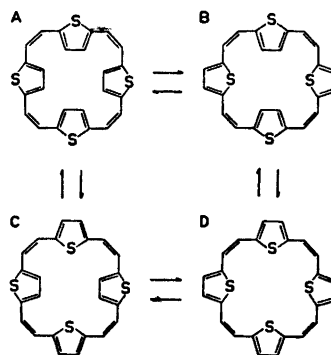
Molecular models show that [2₄](2,5)thiophenophanetetraene should be a rather flexible molecule. A conformation in which the sulfur atoms point outwards from the ring (A in Scheme 2) could be planar enough to allow for some overlap between the *p*-orbitals in the thiophene rings and the olefinic bridges. The thiophene protons are located inside the ring and the olefinic protons outside the ring in this conformation. A delocalized 24 π -electron system should result in a downfield shift of the inner protons and a smaller upfield shift of the outer protons, as is observed in the NMR spectrum of [2₄](2,5)thiophenophanetetraene. The effect, which is enhanced on cooling, is much smaller than in [24]annulene, however.

Table 1. ^1H NMR data of some annulenes, $[2_n]$ cyclophanetrienes (a), and $[2_n]$ cyclophanetetraenes (b).


Compound	Temp. °C	Shift of protons		Remark	Ref.
		outer	inner		
[18]Annulene	20 -60	8.94 9.28	-2.0 -2.99	Diatropic	11
[24]Annulene	40 -80	7.25 4.73	7.25 12.9-11.2	Paratropic	12
a, X=HC=CH X=O X=S	25	H _A 6.79	H _B 6.67	Nonplanar	7, 9
	25	8.68,	8.66 not assigned	Diatropic	8
	25	6.73,	6.67 not assigned	Nonplanar	9
b, X Y HC=CH HC=CH HC=CH S HC=CH O S O S S	25	H _A 6.45	H _B 6.45	No ring-current	1
	25	6.55	6.38		2
	-60	6.58	6.42		
	25	6.34	6.21	Paratropic ?	2
	25	6.17	5.94		
	25	6.19	6.19		
	-60	6.09	6.09	Paratropic	

A conformation in which two sulfur atoms point outwards from, and two towards the center of the cyclophane could be more planar (B and C in Scheme 2). Some deviations from the normal bond angles around the bridging double bonds, of the same magnitude as is observed in $[2_4]$ paracyclophanetetraene,⁵ are necessary, however. Four internal hydrogens and two sulfur atoms could be better accommodated in a planar conformation than eight internal hydrogens (compare A and B in Scheme 2). Such a favoured conformation should well agree with the observed UV spectrum. However, rapid rotation around the single bonds must occur even at -60°C to rationalize the simple NMR spectrum (Scheme 2). The chemical shift for the thiophene protons is then an average of the shift for the internal and external protons. The observed temperature effect is explained by a large paramagnetic shielding of the inner protons and a smaller paramagnetic deshielding of the outer protons.

A conformation in which all four sulfur atoms point towards the center of the cyclophane (D in Scheme 2) could not be planar and show the observed chemical shifts and their temperature dependence.



Scheme 2.

Conclusions. All-*cis* $[2_4](2,5)$ thiophenophane-tetraene or $[2_4]$ annulene tetrasulfide can readily be prepared in a one-step reaction from simple starting materials. Over the 24π -electron periphery, the compound shows a small but significant paramagnetic ring current which is enhanced on cooling. Thus planar conformations have lower energy as is the case

for [24]annulene. Planarity is apparently the most important factor for the delocalization of the π -electrons. The presence of a local aromatic nucleus like thiophene does not interfere with the paratropic behaviour of the molecule.

Experimental. [2₄](2,5)Thiophenophanetetraene, 1. 2,5-Thiophenedicarbaldehyde (5 mmol) and the bistritylphosphonium salt of 2,5-bis(chloromethyl)thiophene (5 mmol) were mixed in dry dimethylformamide (250 ml) in a three-necked flask equipped with a mechanical stirrer and a dropping funnel. The temperature was kept at -40°C with a thermostat-controlled cooling bath, and oxygen-free nitrogen was slowly flushed through the system. Lithium ethoxide in ethanol (ca. 0.3 M) was added dropwise at a rate allowing the coloured ylid to react between successive additions. The rate of reaction was fast in the beginning but slow after ca. half of the required base had been added. The addition took 24 h. When no colour change was observed on addition of base, the reddish solution was warmed to room temperature, diluted with water, and extracted with ether. The ether solution was washed with water, dried, and the solvent evaporated. The residue was chromatographed on silica gel with tetrachloromethane as eluent. The first reddish fractions yielded the desired product, [2₄](2,5)-thiophenophanetetraene, 1 (50 mg, 4.6 %, m.p. $210-215^{\circ}\text{C}$). Later fractions, according to their NMR spectra, contained complex mixtures and were not further investigated. The product was assigned as the all-*cis* isomer. ^1H NMR (270 MHz, CDCl_3): $\delta = 7.32$ and 6.19 (8 H, s, thiophene) (8 H, s, olefin), assigned by comparison with other cyclophanes². On cooling the sample to -60°C , the two singlets separated further to $\delta = 7.57$ and 6.09 . UV (C_6H_{14}): 370 nm (sh), 354 (log $\epsilon = 4.78$) and 298 (4.46). IR (KBr): 1595 cm^{-1} (m), 1445 (m), 1402 (m), 1235 (m), 1108 (m), 842 (m) and 816, 804, 800 (sh), 795 (s). MS (70 eV): m/e 432 (M^+ , 100 %), 399 (4.0), 398 (4.2), 366 (4.4), 365 (5.8), 364 (4.2), 333 (5.1), 332 (3.6) and 216 (M^{2+} , 9.6). Abs. mass 432.0145 ± 0.002 ; calc for $\text{C}_{24}\text{H}_{16}\text{S}_4$ 432.0135.

[2₄]Thiophenophanetetraene, dissolved in cyclohexane or benzene with traces of iodine, was photolyzed in a Rayonet reactor. Light with maximum intensity at 254 or 300 nm was used. Only a slow decomposition of the cyclophane was observed.

[2](2,5)Furano[2](2,5)thiopheno[2](2,5)furano[2](2,5)thiophenophanetetraene, 2, prepared by the above method from 2,5-furandicarbaldehyde and the bistritylphosphonium salt of 2,5-bis(chloromethyl)thiophene, was found to be rather unstable and difficult to purify due to rapid decomposition. ^1H NMR (270 MHz, CDCl_3) of freshly chromatographed sample: $\delta = 7.23$ (4 H, s, thiophene protons), 6.73 (4 H, s, furan protons), 6.19 (4 H, d) and 5.92 (4 H, d, $J = 12.3$ Hz, olefinic protons).

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Preferred Conformational Angles in Peptides Unperturbed by Hydrogen Bonding and α -Substituents

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With the recent X-ray structure determinations of cyclohexasarcosyl¹ and cyclodecasarcosyl,² which turned out to have the configuration sequences, *cis,cis,trans,cis,cis,trans* and *cis,cis,cis,trans,trans,cis,cis,cis,trans,trans*, respectively, some striking common features and