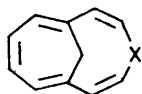


Synthesis of Unsaturated Sulphur Compounds Containing Seventeen- and Twenty-one-membered Rings ¹

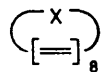
By Terry M. Cresp and Melvyn V. Sargent,* Department of Organic Chemistry, University of Western Australia, Nedlands, W.A. 6009, Australia

The synthesis of 2,5:14,17-diepoxy-8,11-epithiothiacycloheptadecin (12), 2,5:8,11:14,17-triepoxythiacycloheptadecin (13), and 2,5:8,11:12,15:18,21-tetraepoxythiacycloheptadecin (21) is described. The n.m.r. spectra of these compounds show that they are atropic.

REPLACEMENT of one of the double bonds of a $(4n + 2)$ π -electron annulene with a hetero-atom which possesses a lone pair of electrons available for peripheral conjugation will lead to a $(4n + 2)$ π -electron heteroannulene which may be diatropic. Conversely it is expected that replacement of one of the double bonds of a $4n$ π -electron annulene with a hetero-atom may lead to a paratropic system. We were interested in systems which contained rings larger than nine-membered since that case had already been explored.² When we commenced our work in 1970 no monocyclic heteroannulene of this type was known. Since that date this area of research has been one of great activity and methylene-bridged thia- (1) and oxa-cycloundecins (2),³ double-bond isomers of oxacycloheptadecin (3; X = O),⁴ and the ethoxycarbonyl derivative of azacycloheptadecin (3; X = N·CO₂Et)⁵ have been synthesised. None of these systems exhibited any ring current effect in its n.m.r. spectrum. However Sondheimer and his co-workers have observed diamagnetic ring currents for the

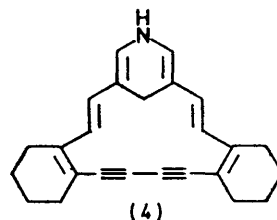


(1) X = S
(2) X = O

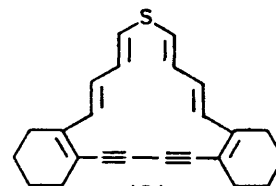


(3) X = O or N·CO₂Et

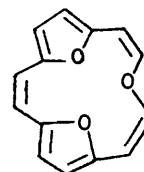
Triepoxy[18]annulene (7)⁸ and diepoxyepithio[18]-annulene (8)⁹ are both planar 18 π -electron systems



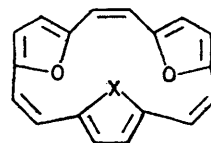
(4)



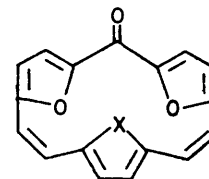
(5)



(6)



(7) X = O
(8) X = S



(9) X = O
(10) X = NH
(11) X = S

azacycloheptadecin (4)⁶ and the thiacycloheptadecin (5).⁶ Japanese workers have described the synthesis of a paratropic diepoxyoxacyclopentadecin (6).⁷

¹ Preliminary communication, T. M. Cresp and M. V. Sargent, *Chem. Comm.*, 1971, 1458.

² S. Masamune and N. Darby, *Accounts Chem. Res.*, 1972, 5, 272; A. G. Anastassiou, *ibid.*, p. 281.

³ E. Vogel, R. Feldmann, H. Düwel, H.-D. Cremer, and H. Günther, *Angew. Chem. Internat. Edn.*, 1972, 11, 217.

⁴ G. Schröder, G. Plinke, and J. F. M. Oth, *Angew. Chem. Internat. Edn.*, 1972, 11, 424.

which are diatropic. The triepoxy[17]annulene (9) and the epiminodiepoxy[17]annulene (10) are planar

⁵ G. Schröder, G. Heil, H. Röttele, and J. F. M. Oth, *Angew. Chem. Internat. Edn.*, 1972, 11, 426.

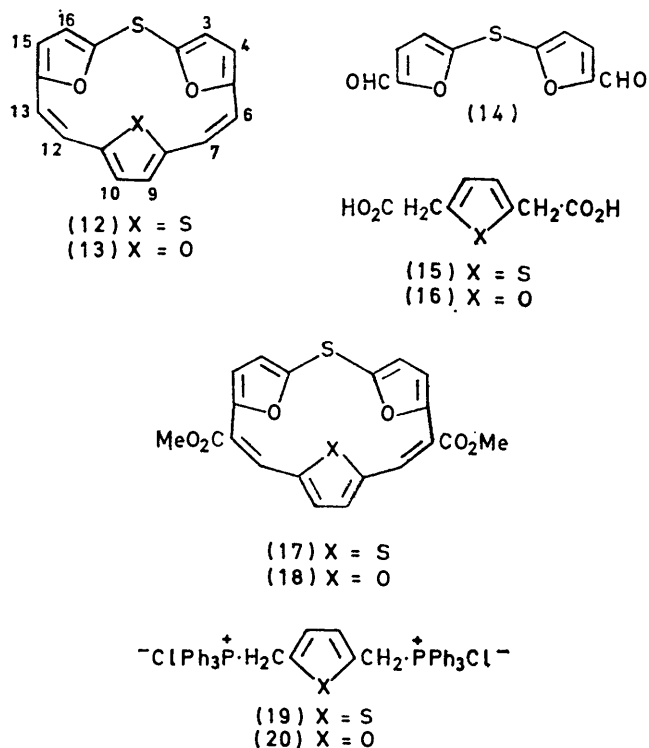
⁶ P. J. Beeby and F. Sondheimer, *J. Amer. Chem. Soc.*, 1972, 94, 2128; *Angew. Chem. Internat. Edn.*, 1972, 11, 833, 834.

⁷ H. Ogawa, M. Kubo, and H. Saikachi, *Tetrahedron Letters*, 1971, 4859.

⁸ G. M. Badger, J. A. Elix, and G. E. Lewis, *Austral. J. Chem.*, 1966, 19, 1221.

⁹ G. M. Badger, G. E. Lewis, and U. P. Singh, *Austral. J. Chem.*, 1966, 19, 1461.

16 π -electron systems which are paratropic, but the diepoxyepithio[17]annulenone (11), in which one of the oxygen bridges in (9) [or the imino-bridge in (10)] has been replaced by a more bulky sulphur atom, no longer exhibits any appreciable paratropicity.¹⁰ We consequently decided to synthesise the diepoxyepithiothiacycloheptadecin (12) and the triepoxythiacycloheptadecin (13).



Perkin-type condensation of the known 5,5'-thiodi-2-furaldehyde (14)¹¹ and thiophen-2,5-diacetic acid (15)¹² gave, after esterification and chromatography, dimethyl 2,5:14,17-diepoxy-8,11-epithiothiacycloheptadecin-7,12-dicarboxylate (17) in 21.3% yield. Hydrolysis and decarboxylation of the ester (17) gave 2,5:14,17-diepoxy-8,11-epithiothiacycloheptadecin (12) in 15.8% yield. Similarly condensation of the dialdehyde (14) with furan-2,5-diacetic acid (16)¹³ gave dimethyl 2,5:8,11:14,17-triepoxythiacycloheptadecin-7,12-dicarboxylate (18) (30.7%) as orange prisms, m.p. 205–206°. Hydrolysis and decarboxylation of ester (18) gave only traces of 2,5:8,11:14,17-triepoxythiacycloheptadecin (13).

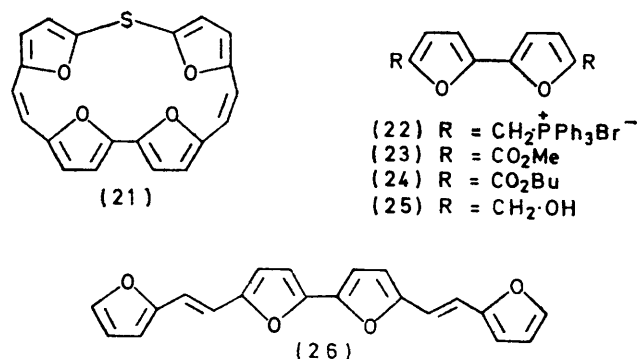
An alternative synthesis of both the macrocycles (12) and (13) was investigated. Thus Wittig reaction between the dialdehyde (14) and thiophen-2,5-diylbis(methylenetriphenylphosphonium chloride) (19)¹⁰ gave the thiacycloheptadecin (12) in 18.7% yield. Similarly the dialdehyde (14) and furan-2,5-diylbis(methylene-

triphenylphosphonium chloride) (20)¹⁰ on Wittig reaction yielded the thiacycloheptadecin (13) in 10.1% yield. In both Wittig reactions triphenylphosphine was also isolated. It presumably arose by a 1,6-elimination from the monoilides, derived from salts (19) and (20), by a mechanism similar to that proposed for the elimination of triphenylphosphine from the monoilide of *trans*-but-2-ene-1,4-diylbis(methylenetriphenylphosphonium bromide).¹⁴

We have also synthesised 2,5:8,11:15:18,21-tetraepoxythiacycloheptadecin (21) by a Wittig route. For this purpose we required 2,2'-bifuryl-5,5'-diylbis(methylenetriphenylphosphonium bromide) (22). Dimethyl 2,2'-bifuryl-5,5'-dicarboxylate (23)¹⁵ was insufficiently soluble in ether or tetrahydrofuran for efficient reduction with lithium aluminium hydride; it was therefore converted into the more soluble dibutyl ester (24). This underwent smooth reduction with lithium aluminium hydride in tetrahydrofuran and afforded the unstable 2,2'-bifuryl-5,5'-dimethanol (25). Attempts to convert the latter into the chloride or the bromide were fruitless. The phosphonium salt (22) was finally obtained in low yield by reaction of the diol (25) with triphenylphosphonium bromide¹⁶ in acetonitrile. Although satisfactory elemental analytical data were not obtained for the salt (22), it behaved in the expected manner in a Wittig reaction. Thus with 2-furaldehyde it yielded *trans,trans*-5,5'-bis-(2-furylvinyl)-2,2'-bifuryl (26).

On Wittig reaction between the aldehyde (14) and the salt (22) the thiacycloheptadecin (21) was obtained in 1.3% yield. All the macrocycles (12), (13), and (21) could be stored in the solid state at 0° for several months without appreciable decomposition.

Examination of Stuart-Briegleb models of the macrocycles indicated that compounds (13) and (21) could



readily adopt a planar conformation, but that the size of the thiophen sulphur atom in compound (12) would probably prevent this system from being planar. We

¹⁰ T. M. Cresp and M. V. Sargent, *J.C.S. Perkin I*, in the press.

¹¹ Z. N. Nazarova and Y. A. Babaev, *Zhur. obshchei Khim.*, 1964, **34**, 4010.

¹² G. M. Badger, J. A. Elix, and G. E. Lewis, *Austral. J. Chem.*, 1965, **18**, 70.

¹³ K. Y. Novitskii, K. Y. Yur'ev, and V. N. Zhingareva, *Zhur. obshchei Khim.*, 1962, **32**, 3303.

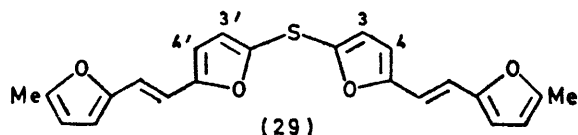
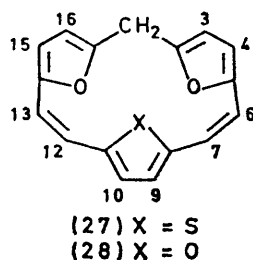
¹⁴ J. A. Ford and C. V. Wilson, *J. Org. Chem.*, 1961, **26**, 1433.

¹⁵ R. Grigg, J. A. Knight, and M. V. Sargent, *J. Chem. Soc. (C)*, 1966, 976.

¹⁶ J. D. Surmatis and A. Ofner, *J. Org. Chem.*, 1963, **28**, 2735.

therefore expected compounds (13) and (21) to exhibit diamagnetic ring currents in their n.m.r. spectra.

As models to assist in determining whether compounds (12), (13), and (21) sustained diamagnetic ring currents we chose the homoannulenes (27) and (28)¹⁰



and the linear system *trans,trans*-5,5'-bis-(5-methyl-2-furylvinyl)-2,2'-thiodifuran (29), which do not show any ring current effect. The latter was synthesised by a Wittig reaction between the dialdehyde (14) and 5-methyl-2-furylmethyltriphenylphosphonium chloride.¹⁰ The n.m.r. spectra of the homoannulenes (27) and (28) serve as models for the chemical shifts of the 6-, 7-, 9-, 10-, 12-, and 13-protons of the thiacycloheptadecins (12) and (13), respectively. The data (Table) show that

N.m.r. chemical shifts (τ values; CDCl_3) for thiacycloheptadecins and homoannulenes

Compound	3-,16-H	4-,15-H	6-,7-,12-,13-H	9-,10-H
(12)	3.37	4.02	3.47, 4.04	3.22
(27) ^a	3.94	4.00	3.62, 3.97	3.20
(13)	3.33	3.95	3.99	3.52
(28) ^a	3.93	4.07	4.23	3.73

^a See ref. 10.

there is no significant difference between the corresponding chemical shifts. The shifts of the 3-, 3', 4-, and 4'-protons of the thiodifuran (29) serve as models for those of the 3-, 16-, 4-, and 15-protons of the thiacycloheptadecins (12) and (13). The 3- and 3'-protons in the thiodifuran (29) resonate at τ 3.38 and the 4- and 4'-protons at τ 3.80. Appropriate comparisons show that again there is no significant difference. Compounds (12) and (13) therefore do not sustain diamagnetic ring currents.

The furan protons of the thiacycloheptadecins (21) resonate as two AB systems centred at τ 3.48 and 3.70, and 3.48 and 3.88, and the olefinic protons give an AB system at τ 4.13 and 4.19. Again this system does not appear to sustain a diamagnetic ring current.

The behaviour of the triepoxythiacycloheptadecins (13), which, unlike the diepoxyepithiothiacycloheptadecins (12), is readily capable of attaining planarity, is thus similar to that of the oxacycloheptadecins (3; X=O)

and the azacycloheptadecins (3; X = N-CO₂Et) synthesised by Schröder and his co-workers.^{4,5} The lack of diatropicity of compound (13) is in marked contrast to the behaviour of the thiacycloheptadecins (5),⁷ which sustains a small diamagnetic ring current. Presumably the perturbations provided by the furan rings in the thiacycloheptadecins (13) prevent any overall peripheral conjugation of the system with participation of the lone pair of electrons on the sulphur atom.

The triepoxy[17]annulene (9), which contains a periphery of 16 π -electrons, is paratropic, and the triepoxy[18]annulene (7), which contains a periphery of 18 π -electrons, is diatropic despite the fact that each possesses the same perturbations as the atropic system (13). This seems to indicate that the ring current in thia-annulenes is less than in either annulenes or annulenes of comparable ring size.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. Light petroleum was a fraction of b.p. 58–65°, and was distilled from phosphorus pentoxide. *NN*-Dimethylformamide was distilled from calcium hydride and stored over 4 Å molecular sieves. Silica gel was B.D.H. 60–120 mesh material. Preparative layer plates (20 × 20 × 0.1 cm) were coated with Merck Kieselgel GF₂₅₄. All phosphonium salts were dried at 56° and 0.01 mmHg before use. Electronic spectra were determined for ethereal solutions, unless stated otherwise, with a Perkin-Elmer 137 spectrophotometer. I.r. spectra were determined for potassium bromide discs, unless stated otherwise, with a Perkin-Elmer 337 grating spectrophotometer. N.m.r. spectra were determined for solutions in deuteriochloroform at 60 MHz with a Varian A-60-A spectrometer, unless stated otherwise. For those determined at 90 MHz a Bruker Spectrospin instrument was used. Molecular weights were determined by mass spectrometry; for low resolution a Varian-M.A.T. CH-7 instrument and for high resolution an A.E.I. MS-902 instrument was used; both instruments were operated at 70 eV.

Dimethyl 2,5:14,17-Diepoxy-8,11-epithiothiacycloheptadecins-7,12-dicarboxylate (17).—A mixture of thiophen-2,5-diacetic acid (15)¹² (1.50 g) and 5,5'-thiodi-2-furaldehyde (14)¹¹ (1.66 g) in acetic anhydride (7.5 ml) and triethylamine (7.5 ml) was set aside at room temperature for 1 h. It was then cooled in ice during the cautious addition of concentrated hydrochloric acid (15 ml). Water (15 ml) was then added and the precipitate was filtered off, washed with a little water, and dried in vacuum to leave a brick-red powder (3.3 g). This was heated under reflux for 2 h in dry methanol (175 ml) containing dry hydrogen chloride (4.7 g) and the solution was poured into water (300 ml). The resulting suspension was extracted exhaustively with chloroform and the extract was washed successively with water, saturated sodium hydrogen carbonate solution, and water, dried (Na₂SO₄), and concentrated. The product was preadsorbed on silica gel and chromatographed over a column of silica gel (total 3.2 × 49 cm) with 10% ethyl acetate-benzene as eluant. Early fractions afforded the *ester* (17) (663 mg, 21.3%), which crystallised from benzene-light petroleum as large brick-red prisms, m.p. 193–195° (Found: M^+ , 414.0230. ¹²C₂₀¹H₁₄¹⁶O₆³²S₂ requires M ,

414.0232); λ_{\max} (CHCl₃) 289 and 296 nm (ϵ 30,500 and 31,300); ν_{\max} (Nujol) 1700 and 1610 cm⁻¹; τ 2.52 (2H, s, 6- and 13-H), 2.90 (2H, s, 9- and 10-H), 3.43 and 3.52 (4H, ABq, $J_{3,4} = J_{15,16} = 3.5$ Hz, 3-, 4-, 15-, and 16-H), and 6.20 (6H, s, Me).

Hydrolysis and Decarboxylation of the Diester (17).—The ester (17) (447 mg) and potassium hydroxide (10 g) were heated under reflux for 1 h in ethanol (50 ml) and water (50 ml). Most of the ethanol was distilled off and the cooled residue was extracted with chloroform. The aqueous layer was acidified with hydrochloric acid and the precipitated dicarboxylic acid was separated, washed with water, and dried in vacuum to leave a brick-red powder (352 mg, 84.5%) which decomposed above 300° without melting. This material and copper chromite (230 mg) were suspended in dry quinoline (4 ml) and heated at 200–205° (bath) for 75 min. The cooled mixture was treated with an excess of cold 10% hydrochloric acid and extracted with ether. The extract was washed successively with 10% hydrochloric acid (3 \times), water (2 \times), and saturated sodium carbonate solution (2 \times), and dried (Na₂SO₄). The residue left on removal of the solvent was preadsorbed from chloroform on silica gel and chromatographed over a column of silica gel (total 2.5 \times 30 cm) with 5% ethyl acetate–light petroleum as eluant. Early fractions afforded 2,5:14,17-diepoxy-8,11-epithiothiacycloheptadecin (12) (50.9 mg, 18.7%), which crystallized from light petroleum as orange blades, m.p. 84.5–85.5° (Found: M^+ , 298.0105. ¹²C₁₆¹⁴H₁₀¹⁶O₂³²S₂ requires M , 298.0122); λ_{\max} 266, 287, and 418 nm (ϵ 25,200, 25,600, and 2700); ν_{\max} 1610, 1390, 1176, 1036, 1010, 1006, 951, 931, 809, 786, and 776 cm⁻¹; τ 3.22 (2H, s, 9- and 10-H), 3.37 and 4.02 (4H, ABq, $J_{3,4} = J_{15,16} = 3.5$ Hz, 3-, 16-, 4-, and 15-H), and 3.47 and 4.04 (4H, ABq, $J_{6,7} = J_{12,13} = 12.0$ Hz, 6-, 7-, 12-, and 13-H).

Dimethyl 2,5:8,11:14,17-Trieoxythiacycloheptadecin-7,12-dicarboxylate (18).—Condensation of furan-2,5-diacetic acid (16)¹³ (5.1 g) and the dialdehyde (14) (4.2 g) in acetic anhydride (22.5 ml) and triethylamine (22.5 ml) gave a brown powder (8.7 g). This was methylated and the crude product was chromatographed as before to yield the ester (18) (2.312 g, 30.7%), which crystallized from benzene–light petroleum as orange prisms, m.p. 205–206° (Found: C, 60.3; H, 3.7%; M^+ , 398. C₂₀H₁₄O₃S requires C, 60.3; H, 3.55%; M , 398); λ_{\max} (CHCl₃) 291 nm (ϵ 24,500); ν_{\max} 3120, 2950, 1700, and 1620 cm⁻¹; τ 2.30 (2H, s, 6- and 13-H), 3.30–3.41 (6H, poorly resolved m, 3-, 4-, 9-, 10-, 15-, and 16-H), and 6.13 (6H, s, Me).

Hydrolysis and Decarboxylation of the Diester (18).—The ester (18) (206 mg) was hydrolysed as before and yielded the dicarboxylic acid (134 mg, 69.9%) as a yellow powder which decomposed above 260° without melting. This material (122 mg) was heated with copper chromite (80 mg) in quinoline (2 ml) at 170–180° (bath) for 1 h and worked up as before. Chromatography of the crude product over a layer plate developed with 5% ethyl acetate–light petroleum yielded the impure thiacycloheptadecin (13) as a yellow-orange solid (2.7 mg), M^+ 282.

2,5:14,17-Diepoxy-8,11-epithiothiacycloheptadecin (12) by Wittig Reaction.—Lithium methoxide [from lithium (69.4 mg)] in dry methanol (24.3 ml) was added during 2 h to a stirred suspension of the dialdehyde (14) (1.11 g) and thiophen-2,5-diylbis(methylenetriphenylphosphonium chloride) (19)¹⁰ (3.53 g) in dry *NN*-dimethylformamide (120 ml) at 90° under dry nitrogen. The solution was then stirred at 90° for a further 2 h, cooled, and poured into

water (600 ml). The mixture was extracted exhaustively with ether and the extract was washed with water (2 \times) and with saturated brine, and dried (Na₂SO₄). Removal of the solvent left a red oil (3.8 g) which was preadsorbed from dichloromethane on silica gel and chromatographed over a column of silica gel (total 4 \times 40 cm) with 10% ethyl acetate–light petroleum as eluant; fractions of 200 ml were collected. Fractions 1 and 2 contained triphenylphosphine (182 mg). Fractions 3–13 contained the product mixed with triphenylphosphine (total 643 mg). The mixture in dry ether (50 ml) was heated under reflux for 6 h with methyl iodide (1 ml). The mixture was cooled and the precipitated phosphonium salt was separated by filtration through kieselguhr and washed with ether. The filtrate was evaporated and yielded the thiacycloheptadecin (12) (279 mg, 18.7%), which crystallized from light petroleum as orange blades, m.p. 84.5–85.5°.

2,5:8,11:14,17-Trieoxythiacycloheptadecin (13) by Wittig Reaction.—Lithium methoxide [from lithium (69.4 mg)] in dry methanol (33.5 ml) was added dropwise during 3 h to a stirred suspension of the dialdehyde (14) (1.11 g) and furan-2,5-diylbis(methylenetriphenylphosphonium chloride) (20)¹⁰ (3.53 g) in dry *NN*-dimethylformamide (125 ml) at 90° under dry nitrogen. The mixture was stirred at 90° for a further 0.5 h and then cooled and poured into water (600 ml). The suspension was extracted exhaustively with ether and the extract was washed with water (2 \times), and with saturated brine, and dried (Na₂SO₄). Removal of the solvent left a red oil (3.9 g) which was preadsorbed from dichloromethane on silica gel and chromatographed over a column of silica gel (total 4 \times 40 cm) with 5% ethyl acetate–light petroleum as eluants; fractions of 200 ml were collected. Fractions 2–5 contained triphenylphosphine (399 mg), and fraction 6 contained triphenylphosphine mixed with a trace of a yellow material. Fractions 7–15 (254 mg) contained the desired product mixed with a little triphenylphosphine. This material in dry ether (50 ml) was heated under reflux for 10 h with methyl iodide (2 ml), cooled, and filtered through a column of silica gel (2.5 \times 18 cm) with ether as eluant. Removal of the solvent from the eluate gave a red gum (142.5 mg, 10.1%) which crystallized from ether–light petroleum to give the thiacycloheptadecin (13), m.p. 95–98°. A sample formed orange prisms from light petroleum, m.p. 97–99° (Found: C, 68.25; H, 3.6%; M^+ , 282. C₁₆H₁₀O₃S requires C, 68.1; H, 3.55%; M , 282); λ_{\max} 253, 296sh, 305, and 417 nm (ϵ 19,600, 30,000, 35,500, and 6000); ν_{\max} 3080, 1620, 1416, 1390, 1180, 1169, 1028, 1016, 1010, 960, 946, 938, 818, and 787 cm⁻¹; τ 3.33 and 3.95 (4H, ABq, $J_{3,4} = J_{15,16} = 3.5$ Hz, 3-, 16-, 4-, and 15-H), 3.52 (2H, s, 9- and 10-H), and 3.99 (4H, s, 6-, 7-, 12-, and 13-H).

Diethyl 2,2'-Bifuryl-5,5'-dicarboxylate (24).—Dimethyl 2,2'-bifuryl-5,5'-dicarboxylate (23)¹⁵ (36.0 g) and sodium hydroxide (20 g) were heated under reflux for 6 h in methanol (260 ml) and water (60 ml). The mixture was cooled in ice and acidified with concentrated hydrochloric acid. The precipitated material was filtered off, washed with water and with ethanol, and dried under vacuum to leave the dicarboxylic acid (28.8 g, 88.7%) as an off-white solid which decomposed at 315° without melting; ν_{\max} (Nujol) 3136, 2690, 2576, 1691, 1576, and 1308 cm⁻¹. The acid (26.5 g) was heated under reflux with stirring in dry butanol (250 ml) containing concentrated sulphuric acid (2 ml). After 18 h the solution was cooled in ice and the crude product was

filtered off, washed with water, and dried under vacuum. The ester (24) crystallised from ether–light petroleum as plates (25.4 g, 70.6%), m.p. 92–95° [raised to 104–106° (from cyclohexane)] (Found: C, 64.55; H, 6.6%; M^+ , 334. $C_{18}H_{22}O_6$ requires C, 64.65; H, 6.65%; M , 334); τ 2.71 and 3.08 (4H, ABq, J 3.5 Hz, 4-, 4'-, 3-, and 3'-H), 5.64 (4H, t, CH_2 ·[CH_2]₂Me), 8.37 (8H, m, CH_2 ·[CH_2]₂Me), and 8.92 (6H, t, Me).

2,2'-Bifuryl-5,5'-diylbis(methylenetriphenylphosphonium bromide) (22).—The dibutyl ester (24) (10.0 g) in dry tetrahydrofuran (150 ml) was added dropwise to a stirred slurry of lithium aluminium hydride (2.5 g) in dry tetrahydrofuran (20 ml). The mixture was then heated under reflux for 1 h, stirred at room temperature for 12 h, cooled in ice, treated with an excess of water, and acidified with dilute hydrochloric acid. The solution was extracted exhaustively with ethyl acetate and the extract washed with saturated sodium hydrogen carbonate solution and with saturated brine, and dried ($MgSO_4$). Removal of the solvent left 2,2'-bifuryl-5,5'-dimethanol (25) (5.76 g, 99.2%) as an off-white solid which decomposed on attempted crystallisation from chloroform, or when kept in light and air for a short time; ν_{max} (Nujol) 3320, 3200, 3120, and 1108 cm^{-1} . A mixture of the foregoing diol (25) (2.48 g) and triphenylphosphonium bromide (8.72 g) was stirred in dry acetonitrile (180 ml) for 5 days at room temperature with the exclusion of light. The precipitate was filtered off, washed with dry ether, and dried under vacuum at 56° to give the phosphonium salt (22) (2.40 g, 22.4%), as an amorphous powder which decomposed at 220° without melting. Attempts to crystallise this material from a variety of solvent systems failed, and the results of elemental analysis were invariably in error (Found: Br, 17.8. $C_{46}H_{38}Br_2O_2P_2$ requires Br, 18.9%).

trans,trans-5,5'-Bis-(2-furylvinyl)-2,2'-bifuryl (26).—Lithium methoxide [from lithium (49.7 mg)] in methanol (24.0 ml) was slowly added dropwise to a stirred suspension of the phosphonium salt (22) (3.0 g) in 2-furaldehyde (1.0 g), and *NN*-dimethylformamide (60 ml) at room temperature under dry nitrogen. After being stirred for a total of 13 h the mixture was poured into water and worked up in the usual way. The crude product was preadsorbed from chloroform on silica gel and chromatographed over a column of silica gel (total 3.5 × 25 cm) with 5% ethyl acetate–light petroleum as eluant to yield the bifuryl (26), which crystallised from benzene–light petroleum as yellow needles (520 mg, 46.0%), m.p. 213–215° (Found: M^+ , 318.0896. $^{12}C_{20}^{14}H_{14}^{16}O_4$ requires M , 318.0892); λ_{max} ($CHCl_3$) 268, 278, 318, and 445 nm (ϵ 23,200, 23,800, 55,000, and 45,100); ν_{max} 3110, 3050, 1475, 1250, 1175, 1141, 1015, 1011, 1005, 958, 952, 918, 906, 880, 797, 779, 740, and 730 cm^{-1} ; τ (90 MHz) 2.61 (2H, m, furan α -H), 3.19 and 3.21 (4H, ABq, J 16.0 Hz, olefinic H), 3.35 and 3.61 (4H, ABq, J 3.5 Hz, bifuryl H), and 3.56–3.68 (m, 4H, furan β -H). Irradiation at the furan α -H frequency gave an AB system due to the furan β -H (J 3.5 Hz).

2,5:8,11:12,15:18,21-Tetraepoxythiacycloheicosin (21).—

Lithium methoxide [from lithium (182 mg)] in dry methanol (66 ml) was added dropwise to a stirred suspension of the phosphonium salt (22) (11.0 g) and the dialdehyde (14) (2.89 g) in dry *NN*-dimethylformamide (200 ml) at room temperature under dry nitrogen. The mixture was stirred for a total of 12 h and then poured into water and worked up in the usual way. The crude product was preadsorbed from chloroform on silica gel and chromatographed over a column of silica gel (total 3 × 44 cm) with 5% ethyl acetate–light petroleum as eluant; fractions of 50 ml were collected. Fractions 1–16 contained triphenylphosphine (144.5 mg). Fractions 17–38 (99.5 mg) were combined and applied to a layer plate which was developed with 5% ethyl acetate–light petroleum. The faster-running orange band yielded an orange solid and the band of lower R_F yielded a yellow solid. Fractions 39–67 (67.3 mg) were rechromatographed over an alumina column (Woelm neutral, activity I, 2 × 24 cm) with 5% ethyl acetate–light petroleum as eluant. Early fractions gave an orange solid and later fractions gave a mixture of two yellow products (t.l.c.) one of which had the same R_F as the yellow solid already mentioned. These yellow products did not have a peak in their mass spectra at the m/e value expected for cyclic products. They darkened rapidly at 0° and were not further investigated. The combined orange solids were crystallised from ether–light petroleum and formed large orange needles of the macrocycle (21) (61.0 mg, 1.3%), m.p. 170–171° (Found: M^+ , 348.0458. $^{12}C_{20}^{14}H_{12}^{16}O_4^{32}S$ requires M , 348.0563); λ_{max} 282, 293sh, 322, and 460 nm (ϵ 44,500, 41,100, and 2600); ν_{max} 3124, 1396, 1195, 1178, 1163, 1096, 1076, 1016, 954, 946, 932, 863, 826, 815, 805, 793, and 746 cm^{-1} ; τ (90 MHz) 3.48 and 3.70 (4H, ABq, J 3.5 Hz, furan H), 3.48 and 3.88 (4H, ABq, J 3.5 Hz, furan H), and 4.13 and 4.19 (4H, ABq, J 12.5 Hz, olefinic H).

trans,trans-5,5'-Bis-(5-methyl-2-furylvinyl)-2,2'-thiodifuran (29).—Lithium methoxide [from lithium (34.7 mg)] in dry methanol (34.2 ml) was added during 0.5 h to a stirred solution of 5-methyl-2-furylmethyltriphenylphosphonium chloride¹⁰ (1.97 g) and the dialdehyde (14) (560 mg) in *NN*-dimethylformamide (100 ml) at 90° under dry nitrogen. After the addition stirring was continued for 1 h and the cooled mixture was poured into water. Work-up in the usual way followed by chromatography of the crude product over silica gel (10% ethyl acetate–light petroleum as eluant) afforded the thiodifuran (29) (583 mg, 61.5%), which crystallised from ether–light petroleum to form yellow prisms, m.p. 118–122° [raised to 126–127° on recrystallisation (4×) from ether] (Found: C, 70.05; H, 4.8%; M^+ , 378. $C_{22}H_{18}O_4S$ requires C, 69.85; H, 4.8%; M , 378); ν_{max} 3100, 2900, 1575, 1555, 1505, 1435, 1352, 1260, 1242, 1161, 1097, 1019, 967, 956, 942, 924, 843, 825, 794, 772, 717, 689, 654, and 635 cm^{-1} ; τ 3.15 and 3.45 (4H, ABq, J 16 Hz, olefinic H), 3.38 and 3.80 (4H, ABq, J 3.5 Hz, 3-, 3'-, 4-, and 4'-H), 3.80 (2H, d, $J_{3,4}$ 3.5 Hz, 3-H of furan ring), 4.03 (2H, dd, $J_{3,4}$ 3.5, $J_{4,Me}$ 1 Hz, 4-H of furan ring), and 7.69br (6H, s, Me).

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