ther experiments to provide additional information relevant to the above are now in progress.

Acknowledgment. Jay H. Worrell wishes to acknowledge financial support for this work from a Research Corporation, Frederic Gardner Cottrell Project Grant, and a release time award from the University of South Florida Research Council.

(13) Address correspondence to this author.

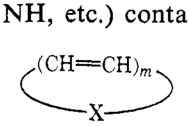
Jay H. Worrell,[13] Jack J. Genova
Department of Chemistry, The University of South Florida
Tampa, Florida 33620

Received June 2, 1970

The Synthesis of Fully Unsaturated 11-, 12-, and 13-Membered Sulfur Heterocycles[1]

Sir:

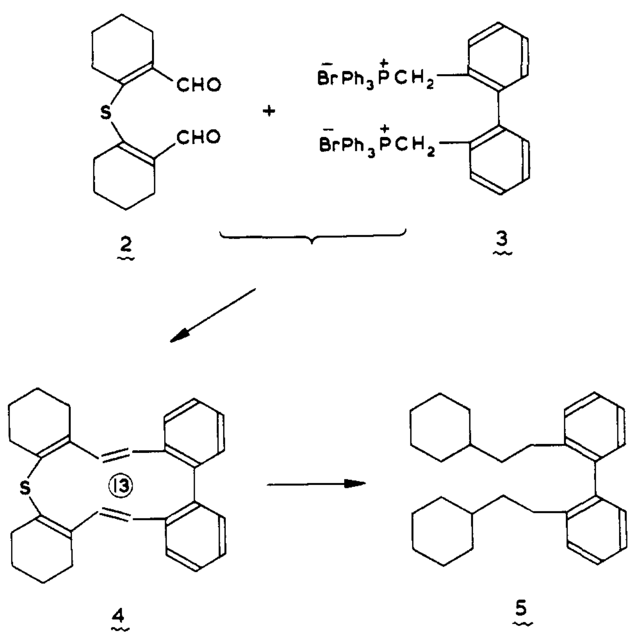
No fully unsaturated monocyclic monoheterocycle (type **1**, X = S, O, NH, etc.) containing a ring larger


$$\overbrace{(CH{=}CH)_m}\ \text{ring with } X$$

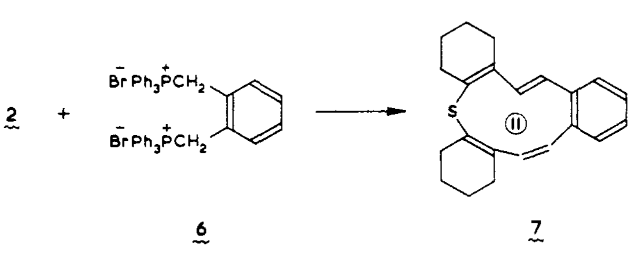
1

than the nine-membered one (m = 4) appears to be known. It was of interest to synthesize macrocyclic members of this series, in order to determine the properties of these higher homologs of thiophene, furan, and pyrrole (m = 2). The possibility existed that they would be aromatic when m = 6, 8, 10, etc. and nonaromatic when m = 5, 7, 9, etc., in the same way as certain [4n + 2]annulenes have been shown to be aromatic and [4n]annulenes nonaromatic.[2] In order to test this possibility, we have prepared the 13-membered sulfur heterocycle **4** (a fused derivative of **1**, X = S, m = 6), as well as the 11-membered sulfur heterocycle **7** (a fused derivative of **1**, X = S, m = 5). The 12-membered ring sulfur compound **9** has also been synthesized.

Wittig reaction of 2,2′-thiodi-1-cyclohexene-1-carboxaldehyde (**2**)[3,4] and 2,2′-bis(triphenylphosphoniomethyl)biphenyl dibromide (**3**)[5] in dimethylformamide with ethanolic lithium ethoxide at 90°[6] led to a mixture of products, from which *trans,trans*-dibenzo[*f,h*]dicyclohexeno[*b,l*]thiacyclotridecahexaene (**4**)[7] was isolated in 12% yield[8] by chromatography on alumina and then tlc on kieselgel. Substance **4** formed colorless crystals, mp 113–115°;[9] mass spectrum, molecular ion at m/e 396; uv max (C_6H_{12}) ~246 sh (ε 19,000), 291 (19,900), and 343 nm (20,800); ir (KBr) 965 s cm^{-1} (*trans*-olefin). The nmr spectrum of **4** (100 MHz, $CDCl_3$) confirmed the assigned structure and stereochemistry, showing signals at τ 2.10–2.50 (m, 2 H), 2.60–3.10 (m, 8 H) (benzenoid and olefinic), 3.74 (broadened d, J = 16.5 Hz, 2 H, olefinic), 7.60–8.15 (broad d, 8 H, allylic methylene), and 8.20–8.65 (broad s, 8 H, nonallylic methylene). Further confirmation for structure **3** was obtained by desulfurization with Raney nickel in ethyl acetate under hydrogen at room temperature (2 hr), which led to 2,2′-di(β-cyclohexylethyl)biphenyl (**5**) as a colorless liquid; mass spectrum, molecular ion at m/e 374; uv max (C_6H_{12}) 264 (ε 940) and 271 nm (800);[10] nmr (60 MHz, CCl_4) τ 2.65–3.15 (m, 8 H, benzenoid), 7.50–8.10 (m, 4 H, benzylic methylene), and 8.20–9.65 (m, 26 H, methylene and methine).



Reaction of the aldehyde **2** and *o*-xylylenebis(triphenylphosphonium bromide) (**6**)[6,11] with lithium ethoxide under the previously mentioned conditions,[6] followed by separation as before, gave *cis,trans*-benzo[*f*]dicyclohexeno[*b,j*]thiacycloundecapentaene (**7**) in



2.2% yield. This substance formed colorless needles, mp 130–132°;[9] mass spectrum, molecular ion at m/e 320; uv max (C_6H_{12}) 237 (ε 31,000), ~290 sh (7300), 330 (5600), and ~348 sh nm (4300); ir (KBr) 985 s cm^{-1} (*trans*-olefin). The nmr spectrum of **7** (100 MHz, $CDCl_3$) again confirmed the assigned structure and stereochemistry, showing signals at τ 2.30–2.50 (m, 1 H),

---

(1) Unsaturated Macrocyclic Compounds. LXXI. For part LXX, see E. P. Woo and F. Sondheimer, *Tetrahedron*, in press.

(2) See F. Sondheimer, I. C. Calder, J. A. Elix, Y. Gaoni, P. J. Garratt, K. Grohmann, G. di Maio, J. Mayer, M. V. Sargent, and R. Wolovsky, *Chem. Soc. Spec. Publ.*, No. 21, 75 (1967).

(3) M. Weissenfels and M. Pulst, *Tetrahedron Lett.*, 3045 (1968).

(4) For syntheses of other cyclic sulfur compounds by the Wittig reaction of **2**, see P. J. Garratt, A. B. Holmes, F. Sondheimer, and K. P. C. Vollhardt, *J. Amer. Chem. Soc.*, **92**, 4492 (1970).

(5) (a) D. M. Hall and B. Prakobsantisukh, *J. Chem. Soc.*, 6311 (1965); (b) H. J. Bestmann, H. Häberlein, H. Wagner, and O. Kratzer, *Chem. Ber.*, **99**, 2848 (1966); (c) E. D. Bergmann, P. Bracha, I. Agranat, and M. A. Kraus, *J. Chem. Soc. C*, 328 (1967).

(6) See C. E. Griffin and J. A. Peters, *J. Org. Chem.*, **28**, 1715 (1963).

(7) The cis,trans isomer of **4** appeared also to be formed, but was not obtained pure.

(8) Essentially the same yield of **4** was obtained when **3** was first converted to the corresponding bisylide with sodamide in liquid ammonia, followed by reaction with **2** in boiling benzene–ether.

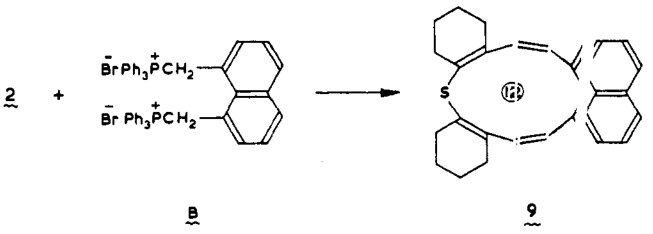
(9) Satisfactory elemental analyses were obtained for all new crystalline compounds.

(10) By comparison, 2,2′-dimethylbiphenyl shows uv max (95% EtOH) 263.5 (ε 800) and 271 nm (600) [P. M. Everitt, D. M. Hall, and E. E. Turner, *J. Chem. Soc.*, 2286 (1956)].

(11) C. E. Griffin, K. R. Martin, and B. E. Douglas, *J. Org. Chem.*, **27**, 1627 (1962).

2.60–2.85 (m, 3 H) (benzenoid), an AB quartet at 3.20 and 3.38 (J_{AB} = 12 Hz, 2 H, *cis*-olefinic), an AB quartet at 3.65 and 3.82 (J_{AB} = 16.5 Hz, 2 H, *trans*-olefinic), 7.45–7.85 (broad s, 8 H, allylic methylene), and 7.95–8.35 (broad s, 8 H, nonallylic methylene).

1,8-Bis(triphenylphosphoniomethyl)naphthalene dibromide (**8**)[5b,12] was converted to the corresponding bisylide with sodamide in liquid ammonia,[12b] followed by treatment with the dialdehyde **2** in boiling ether–benzene. Chromatography on alumina gave 2% of *cis,cis*-naphtho[1,9,8-*fg*]dicyclohexeno[*b,k*]thiacyclododecapentaene (**9**) as colorless needles, mp 138–140°;[9] mass spectrum, molecular ion at *m/e* 370; uv max (95% EtOH) 239 (ε 37,000), 322 (8800), and ~338 sh nm (7600); ir (KBr), only weak bands (at 948, 958, 978, and 988 cm^{-1}) in the 920–1000-cm^{-1} region. Assignment of the cis,cis stereochemistry is based on the ir spectrum and the nmr spectrum (100 MHz, $CDCl_3$), which showed signals at τ 2.30–2.55 (m, 2 H) and 2.60–2.90 (broad d, 4 H) (benzenoid), an AB quartet at 3.31 and 3.67 (J_{AB} = 12 Hz, 4 H, *cis*-olefinic), and 7.70–9.25 (m, 16 H, methylene).



The nmr spectra of **4**, **7**, and **9** indicate no appreciable ring current effects due to the macrocyclic rings, and presumably they are nonplanar molecules. The fact that the 13-membered ring compound **4** (type **1**, *m* = 6) shows no sign of aromaticity parallels the behavior of fully unsaturated nine-membered heterocycles (type **1**, *m* = 4) containing an S,[4,13] O,[13,14] or NCOOEt[15] grouping, but not that of 1*H*-azonine[16] which contains an NH grouping.

Acknowledgments. One of us (A. B. H.) is indebted to the Shell Company of Australia for a postgraduate scholarship.

[12] (a) E. D. Bergmann and I. Agranat, *J. Org. Chem.*, **31**, 2407 (1966); (b) R. H. Mitchell and F. Sondheimer, *Tetrahedron*, **24**, 1397 (1968).

[13] A. P. Bindra, J. A. Elix, P. J. Garratt, and R. H. Mitchell, *J. Amer. Chem. Soc.*, **90**, 7372 (1968).

[14] A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 903, 1521 (1969); S. Masamune, S. Takada, and R. T. Seidner, *J. Amer. Chem. Soc.*, **91**, 7769 (1969).

[15] A. G. Anastassiou and J. H. Gebrian, *ibid.*, **91**, 4011 (1969); *Tetrahedron Lett.*, 5239 (1969); S. Masamune, K. Hojo, and S. Takada, *Chem. Commun.*, 1204 (1969).

[16] A. G. Anastassiou and J. H. Gebrian, *Tetrahedron Lett.*, 825 (1970).

[17] To whom correspondence should be addressed.

A. B. Holmes, F. Sondheimer[17]
Chemistry Department, University College
London W.C.1, England

Received May 13, 1970

Ordered Structures in Sequential Copolypeptides Containing L-Proline or 4-Hydroxy-L-proline[1]

Sir:

Ordered structures in sequential copolytripeptides and copolyhexapeptides containing L-proline and glycine have been detected in the solid state[2] and in solution.[3,4] Copolypeptides with glycine at every third residue, which is a strict steric requirement for the formation of the collagen triple helix,[5,6] have been most frequently studied. We have observed that sequential copolypeptides which do not contain glycine as every third residue may nevertheless develop order in dilute solution.

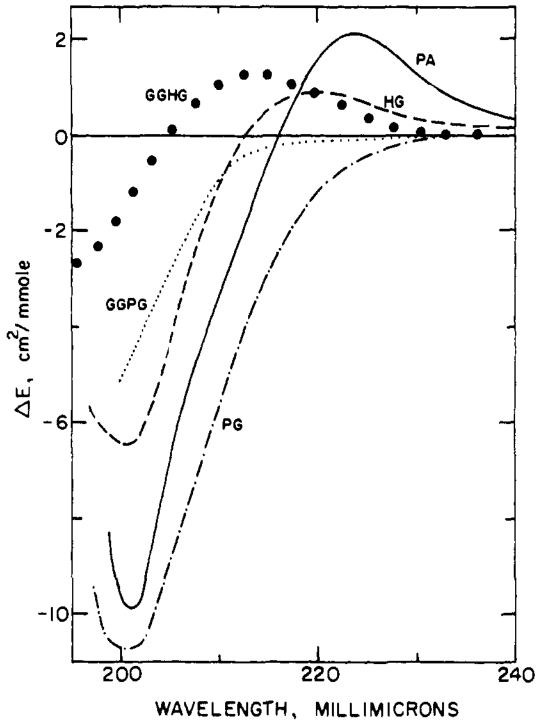


Figure 1. Circular dichroism of PA (——) at −42°, GGPG (......) and GGHG (●●●) at −45°, and PG (–·–·–) and HG (– – –) at −48° in 2:1 ethylene glycol–water.

Poly(L-prolyl-L-alanine) (PA), M_W = 3000, poly(L-prolylglycine) (PG), M_W = 13,200, poly(4-hydroxy-L-prolylglycine) (HG), M_W = 10,400, poly(glycylglycyl-L-prolylglycine) (GGPG), M_W = 6700, and poly(glycylglycyl-4-hydroxy-L-prolylglycine) (GGHG), M_N = 9400, exhibit only negative circular dichroism (CD) over the accessible spectral region in water at 75–85°. The minimum is at 196–198 mμ for GGHG, 204–205 mμ for PA, and close to 200 mμ for PG, HG, and GGPG, with an average CD per peptide bond of about −2 cm²/mmol for GGPG and GGHG and about −6 cm²/mmol for PA, PG, and HG. These spectra are qualitatively similar to that of heat-denatured collagen, which shows a broad minimum at 195–198 mμ with $\Delta E = -4$ cm²/mmol.[7] However, as is shown in Figure 1, major differences appear in the CD obtained at low temperatures in ethylene glycol–water mixtures. Although PG and GGPG still exhibit

---

[1] This work was supported by a contract with the Division of Biology and Medicine, Atomic Energy Commission.

[2] D. M. Segal, W. Traub, and A. Yonath, *J. Mol. Biol.*, **43**, 519 (1969), and references therein.

[3] F. R. Brown, III, J. P. Carver, and E. R. Blout, *ibid.*, **39**, 307 (1969).

[4] Y. Kobayashi, R. Sakai, K. Kakiuchi, and T. Isemura, *Biopolymers*, **9**, 415 (1970), and references therein.

[5] G. N. Ramachandran and G. Kartha, *Nature* (*London*), **176**, 593 (1955); G. N. Ramachandran and V. Sasisekharan, *Biochim. Biophys. Acta*, **109**, 314 (1965).

[6] A. Rich and F. H. C. Crick, *Nature* (*London*), 176, 915 (1955); *J. Mol. Biol.*, **3**, 483 (1961).

[7] M. L. Tiffany and S. Krimm, *Biopolymers*, **8**, 347 (1969).