nm. The agreement at 245 nm is less satisfactory, but observed relative magnitudes of the three components of $\epsilon_L - \epsilon_R$ are in good accord with theory.

The fact that the value of $\Delta\theta/\theta$ at the 275-nm band is slightly less than that at the 245-nm band suggests the existence of a weak n → π^* transition[11,14] with positive rotational strength in the 275-nm band region; this would contribute to θ_{11} and θ_{22}.

These studies are being continued with other polynucleotide systems.

Acknowledgment. We are grateful to I. Tinoco, Jr., for helpful comments.

(14) K. Kasha in "Light and Life," W. D. McElroy and B. Glass, Ed., Johns Hopkins University Press, Baltimore, Md., 1960, p 31.

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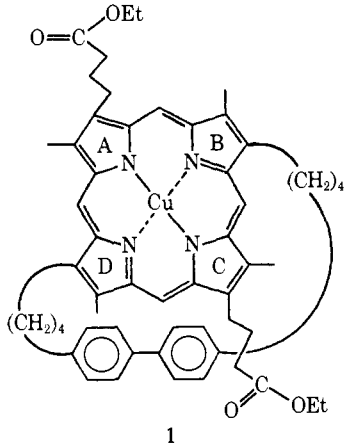
Cyclophane Porphyrin[1]

Sir:

We report the synthesis of copper 1,3,5,7-tetramethyl-2,6-di-γ-carbethoxypropyl-4,8-(biphenyl-4,4′-ditetramethyleno)porphyrin (**1**), a cyclophane metallo-



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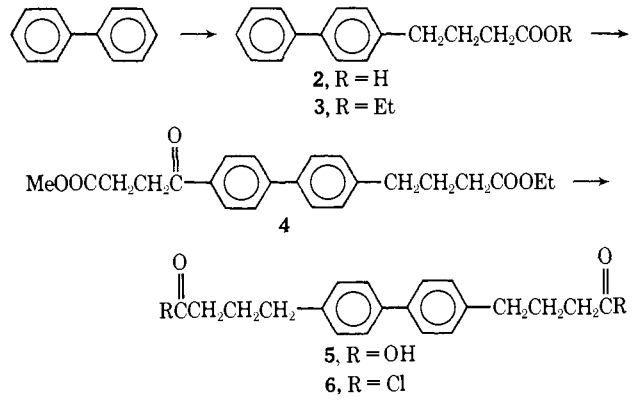
porphyrin. This compound was prepared as part of an effort to synthesize the active site in myoglobin or hemoglobin, without the accompanying protein. We conjectured that if the proper environment such as a histidine molecule on one side and a hydrophobic environment on the other side of the ferroheme[2] were assembled, the molecule might reversibly bind oxygen. These two features would be incorporated by converting **1** into a histidyl derivative of the corresponding ferroporphyrin. A successful implemention of this idea would provide much information concerning the function of the large proteins in enzymatic catalysis and also allow a detailed study of the mechanism of reversible oxygen binding.

After unsuccessful attempts to synthesize the cyclophane porphyrin by building a cyclophane ring system, $-(CH_2)_n$–aromatic–$(CH_2)_n-$, onto a porphyrin, we adopted the more tactical approach of constructing the porphyrin through dipyrromethenes which were attached to both ends of an aromatic system. The intramolecular porphyrin condensation takes advantage of copper(II) ion chelation to fix the dipyrromethene ends in a proper position for bond formation between the dipyrromethene containing rings A and D and that containing rings B and C in **1**.

Biphenyl was converted into γ-(4-biphenyl)butyric acid (**2**) (mp 118°) by Friedel–Crafts reaction with succinic anhydride,[3,4] followed by a Wolff–Kishner reduction. Esterification gave the ethyl ester **3**. Friedel–



Crafts reaction of **3** and β-carbomethoxypropionyl chloride[5] gave 4-(γ-carbethoxypropyl)-4′-(β-carbomethoxypropionyl)biphenyl (**4**) (mp 68°) in 70% yield. Hydrolysis of the ester and reduction of the carbonyl group by Wolff–Kishner reaction carried out in triethylene glycol gave biphenyl-4,4′-dibutyric acid (**5**) (mp 185°). The overall yield to this step was 22% based on biphenyl. Treating the acid **5** with thionyl chloride gave biphenyl-4,4′-dibutyric acid chloride (**6**), mp 72–73°.

Formation of bis[*p*-phenylenetrimethylenecarbonyl-(2,4-dimethyl-5-carbethoxypyrrol-3-yl)] (**8**) was accomplished by Friedel–Crafts acylation of 2,4-dimethyl-5-carbethoxypyrrole (**7**)[6,7] with the acid chloride (**6**) in the presence of 4 equiv (based on pyrrole) of anhydrous aluminum chloride in nitrobenzene.[8] After work-up and recrystallization from acetone, **8**, mp 192°, was obtained in 59% yield.[9] Reduction of **8** with diborane[10] in tetrahydrofuran gave bis[*p*-phenylenetetramethylene-(2,4-dimethyl-5-carbethoxypyrrol-3-yl)] (**9**), mp 164–165°. The benzyl ester **10** was prepared by transesterification of **9** in the presence of sodium benzyloxide. In order to obtain bis[*p*-phenylenetetramethylene(2-

(1) This work was supported by a grant from the National Institutes of Health (AM 11404).

(2) J. H. Wang, *Accounts Chem. Res.*, 3, 90 (1970), and references cited therein.

(3) (a) M. Weizmann, E. Bergmann, and E. Bogradov, *Chem. Ind. (London)*, **59**, 402 (1940); (b) D. H. Hey and R. Wilkinson, *J. Chem. Soc.*, 1030 (1940).

(4) We list analyses and spectra for key intermediates. However, nmr spectra of all intermediates are consistent with structures written.

(5) J. Cason, "Organic Syntheses," Collect. Vol. 3, Wiley, New York, N. Y., 1955, p 169.

(6) (a) H. Fischer, "Organic Syntheses," Collect. Vol. 2, Wiley, New York, N. Y., 1943, p 202; (b) A. H. Corwin and W. M. Quattlebaum, Jr., *J. Amer. Chem. Soc.*, **58**, 1081 (1936).

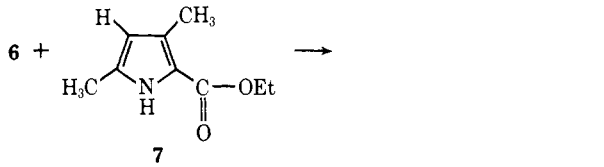
(7) H. Fisher and H. Orth, "Die Chemie des Pyrrols," Vol. I, Akademie Verlag, Leipzig, 1934, p 239.

(8) H. Fischer and F. Schubert, *Z. Physiol. Chem.*, **155**, 110, 1 (1926).

(9) *Anal.* Calcd, for $C_{38}H_{48}N_2O_4$: C, 76.47; H, 8.11; N, 4.70. Found: C, 76.33; H, 8.28; N, 4.80. For the nmr spectrum ($CDCl_3$), see Table I.

(10) (a) K. M. Biswas, L. E. Houghton, and A. H. Jackson, *Tetrahedron, Suppl.*, 7, 261 (1966); (b) T. A. Ballantine, A. H. Jackson, G. W. Kenner, and G. McGilivray, *ibid.*, 7, 241 (1966).

formyl-4-methyl-5-carbobenzoxypyrrol-3-yl)] (**11**), **10** was first treated with sulfuryl chloride, then with dimethylamine. Hydrolysis of the immonium salt gave the aldehyde[11] **11**, mp 183°. Catalytic hydrogenolysis of **11** with 5% palladium/charcoal[12] converted the benzyl ester to the acid **12** in near quantitative yield.



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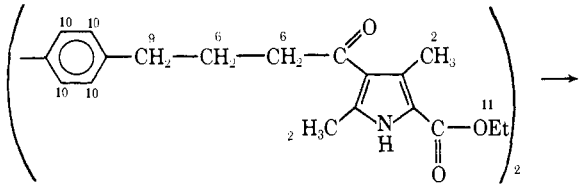

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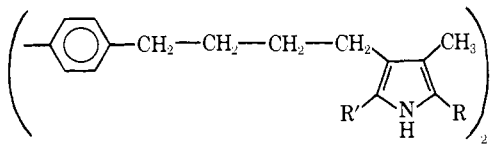
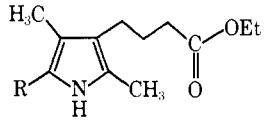
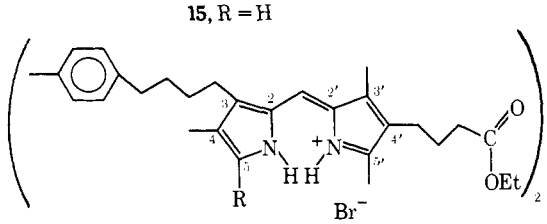


9, R′ = CH_3; R = COOEt
10, R′ = CH_3; R = $COOCH_2Ph$
11, R′ = CHO; R = $COOCH_2Ph$
12, R′ = CHO; R = COOH

2,4-Dimethyl-3-(γ-carbethoxypropyl)pyrrole (**15**) (bp 129° (3 mm)) was prepared from **13**[13,14] by catalytic hydrogenolysis to **14** and subsequent decarboxylation.

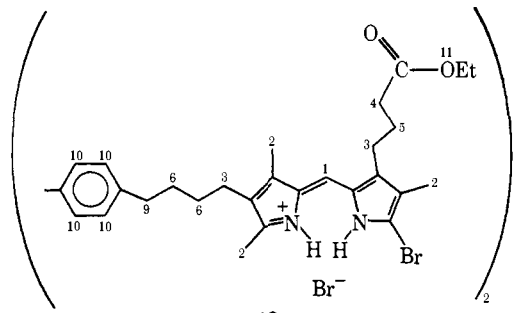


13, R = $COOCH_2Ph$
14, R = COOH
15, R = H



16, R = COOH
17, R = Br

Condensation of the formyl group of **12** with **15** using HBr in acetic acid[15] afforded bis[*p*-phenylenetetramethylene(4,3′,5′-trimethyl-4′-γ-carbethoxypropyl-5-carboxy-2,2′-dipyrromethene-3-yl)hydrobromide] (**16**). Treatment of **16** with bromine in acetic acid gave the corresponding 5-bromo compound **17**.[16] Stirring a solution of **17** in chloroform–ethanol containing ammonia and $Cu(OAc)_2 \cdot H_2O$ gave the orange-brown copper(II) complex[17] **21**. A comparison of the



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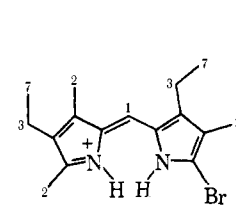

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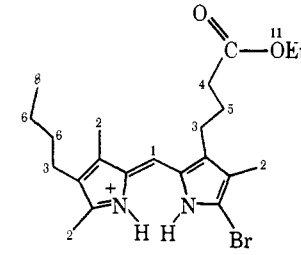

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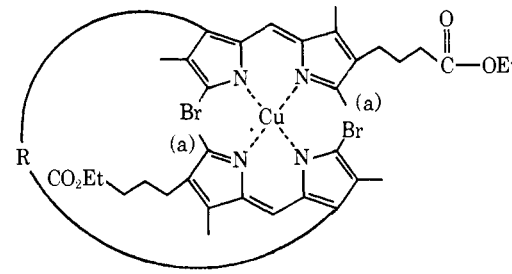

21, R = $-(CH_2)_4-$ $-(CH_2)_4-$

uv–visible spectra of the dipyrromethenes, their hydrobromides, and the related copper complexes (Table I) with those of known structures clearly identifies our intermediates as having the indicated chromophores. The nmr data (Table II) identify the structures. The free base related to **17** moved rapidly as a single spot upon thin-layer chromatography as did the final copper porphyrin described below. This behavior excludes polymeric structures.

Heating the xylene solution of **21** with triethylamine[17a] at 125° for 2 hr gave a dark brown mixture.[18]

(11) A. H. Jackson, G. W. Kenner, and D. Warburton, *J. Chem. Soc.*, 1328 (1965).

(12) (a) E. Bullock, A. W. Johnson, E. Markham, and K. B. Shaw, *ibid.*, 1430 (1958); (b) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, Chapter 1.

(13) 2,4-Dimethyl-3-(γ-carbethoxypropyl)-5-carbobenzoxypyrrole (**13**) was prepared by condensation of nitrosated benzyl acetoacetate and ethyl 5-acetyl-6-oxoheptanoate according to standard literature procedures.[14]

(14) A. W. Johnson, E. Markham, R. Price, and K. B. Shaw, *J. Chem. Soc.*, 4254 (1958).

(15) Reference 6a, p 36.

(16) Reference 6a, p 62.

(17) (a) A. H. Corwin and V. L. Sydow, *J. Amer. Chem. Soc.*, **75**, 4484 (1953); (b) A. W. Johnson, I. T. Kay, E. Markham, R. Price, and K. B. Shaw, *J. Chem. Soc.*, 3416 (1959).

(18) We had previously synthesized the copper complex derived from **18**, which is like **21**, but having the R and the butyric acid esters interchanged. This resulted in a configuration having the CH_3 groups at site a in **21** very close to the aromatic ring as shown below and possibly

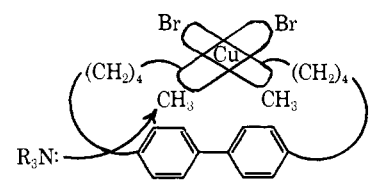

Table I. Uv-Visible Spectra of Dipyrromethenes, Dipyrromethene Hydrobromides, and Copper Chelates Derived from These Intermediates

Compd	λ_{max}, mμ[c]	ε, l. mol^{-1} cm^{-1}
19[a]	369	11,300
	465 sh	
	493	85,000
20[b]	369	8,500
	464 sh	
	493	91,000
18	254	33,400
	262 sh	
	370	17,600
	465 sh	
	493	164,000
17	260	33,000
	330	10,500
	465 sh	
	491	72,600
Cu^{II} chelate derived from **19**	333	9,800
	(398)	12,400
	474 ssh	
	493	49,000
	519 ssh	
Free base derived from **19**	338	4,800
	474	42,900
Cu^{II} chelate derived from **20**	(400)	
	469	s
	495 ssh	
	519	
Free base derived from **20**	344	4,300
	482	38,000
Cu^{II} chelate derived from **18**	264 ssh	
	(402)	
	470	s
	492 sh	
	517	s
Cu^{II} chelate derived from **17**	260	s
	330	w
	470	s
	519	s
Free base derived from **17**	338	w
	481	s

[a] Identified with that reported by H. Fischer, *Justus Liebigs Ann. Chem.*, **475**, 221 (1929). [b] Every step in the synthesis reported here was duplicated in a simple porphyrin synthesis. The compound **20** is an intermediate in a model synthesis. The C, H, N, and Br analyses agree with the structure indicated. [c] s = strong, w = weak, sh = shoulder, ssh = strong shoulder. These symbols are used where concentrations were not determined.

Work-up by repeated chromatography through silica gel gave a pink solution which showed in the uv and visible spectrum typical bands for copper porphyrins, *i.e.*, 562 (ε 23,000) (α band), 524 (ε ≅ 10,000) (β band), and 399 mμ (ε 310,000) (Soret band), and an additional intense absorption around 265 mμ (ε ≅ 300,000) (biphenyl). The yield was about 5%. Mass spectrum showed a parent peak at 917, the calculated molecular weight of the copper porphyrin **1**. The increase in extinction coefficient at 265 mμ from 33,000 to 300,000 in going from **17** to the porphyrin **1** is typical of flattening a biphenyl system and supplies further evidence for the cyclophane structure of **1**.

By shaking the chloroform solution of the copper porphyrin with 10 *M* H_2SO_4[19] we obtained the free porphyrin with uv and visible absorption bands at 610 (broad and weak), 562, 528, 496 (strongest in the visible four-band series), 399 (Soret), and 265 mμ. Treatment of this porphyrin by the usual ferrous sulfate procedure[20] gave a violet solution with the uv-visible spectrum expected for Fe(III) porphyrins.

Conversion of **1** to the corresponding histidyl ferroporphyrin and alternate procedures to improve the yields of **1** are underway.

Acknowledgment. We are grateful to the National Institutes of Health for financial support, and to Professors David Mauzerall and David A. Lightner for helpful advice and assistance.

resulted in severe steric interference with the amine-catalyzed ring closure. No porphyrin could be obtained. Substitution of less-hindered bases, *e.g.*, DABCO and DBN for trimethylamine, gave about 0.1% yield of the copper porphyrin **1**. In model systems, *e.g.*, using **20**, the yield of porphyrin is 15–20%.

(19) Treatment with concentrated H_2SO_4 resulted in decomposition of the cyclophane porphyrin.

Table II. Nmr Spectra of Some Intermediates[a]

Proton(s) (see structures in Table I)	**19**	**20**	**18**	**8**
N–H	−3.28, −3.38 b	−3.24, −3.36 b	−3.23, −3.35 b	0.58 b
1	2.93 s	2.80 s	2.76 s	
2	7.32 s	7.30 s	7.30 s	7.35 s
	7.68 s	7.63 s	7.65 s	7.65 s
	7.98 s	7.96 s	7.94 s	
3	7.26 q	7.17 t	7.16	
	7.53 q	~7.55	~7.5–7.55	
4		7.6–7.7	7.6–7.7	
5		~8.25 m	~8.25 m	
6		~8.55 m	~8.4 m	~8.2 m
7	8.83 t			~7.7
	8.93 t			
8		9.04 t		
9			≈7.35	~7.5 m
10			2.58 (AB spectrum)	2.58
11 (Et)		5.83 q	5.83 q	5.83 q
		8.73 t	8.73 t	8.73 t

[a] All spectra were taken in $CDCl_3$. Chemical shifts are given in τ values (10 − δ). Resonances for which only approximate τ values are listed could not be determined accurately because of superposition with other resonances; b = broad, s = singlet, t = triplet, q = quartet, m = multiplet.

(20) J. E. Falk, "Porphyrins and Metalloporphyrins," Elsevier, New York, N. Y., 1964, p 133.

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Received February 20, 1971

Olefin Inversion by the Phosphorus Betaine Method

Sir:

We wish to describe a stereospecific method for synthesis of phosphorus betaines and application of this method for facile inversion of olefin stereochemistry. Previous examples of betaine generation include the classical Wittig reaction of alkylidenetriphenylphosphoranes with carbonyl compounds,[1] deprotonation of β-hydroxyphosphonium salts,[2] and reaction of epoxides or ethylene carbonates with trisubstituted phosphines.[3]

(1) A. W. Johnson, "Ylid Chemistry," Academic Press, New York, N. Y., 1966, Chapter 4.

(2) (a) M. E. Jones and S. Trippett, *J. Chem. Soc. C*, 1090 (1966); (b) G. Wittig and U. Schollkopf, *Chem. Ber.*, **87**, 1318 (1954).

(3) (a) G. Wittig and W. Haag, *ibid.*, **88**, 1654 (1955); (b) M. J. Boskin and D. B. Denney, *Chem. Ind. (London)*, 330 (1959); (c) A. J.