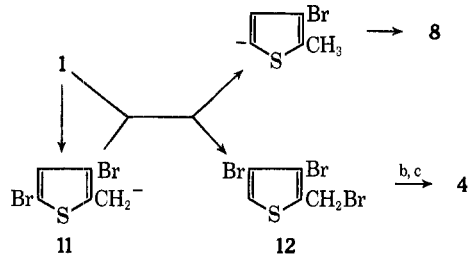
These results suggest that side-chain bromination requires that more than one bromine atom be attached to the thiophene ring. A possible mechanism for this reaction which is consistent with this observation as well as our previous investigations[2] involves initial formation of a thenyl carbanion **11** in which the negative charge is partially stabilized by the cumulative inductive effects of the bromine atoms. This carbanion attacks a labile[10] α-bromine atom of a bromothiophene



such as **1** to generate thenyl bromide **12** and the dehalogenated thiophene **8**.

Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were taken as films or KBr disks on a Beckman IR-10 or a Perkin-Elmer 237 instrument and were calibrated with a polystyrene film. Nmr spectra were obtained with a Varian A-60A instrument and calibrated with TMS as an internal reference. A Finnegan 1015SL quadrupole mass spectrometer was used for the mass spectrum determination. Gas chromatographic analysis was carried out on an Aerograph Autoprep A-700 using a 14 ft × 0.25 in. column of 20% DC QF-1 on Chromosorb W. Analyses were performed at M-H-W Laboratories, Garden City, Mich.

Reaction of 2-Methyl-3,5-dibromothiophene (1) with Potassium Amide.—Following the previously described procedure,[3] 5.2 g (0.02 mol) of **1** was treated with 0.12 mol of KNH_2 in 150 ml of liquid NH_3 for 15 min. After the usual work-up procedure,[3] the neutral fraction consisted of 0.5 g (14%) of 4-bromo-2-methylthiophene (**3**) identified by a comparison of its infrared spectrum with that of an authentic sample.[3] The basic fraction was acetylated and worked up as previously described[3] to give 0.71 g (15%) of the thenylacetamide **6**, mp 89–89.5°, whose infrared and nmr spectra were identical with those of a synthetic sample prepared as described below.

A vpc analysis of the neutral fraction from a similar reaction carried out at −60° showed the presence of starting material **1** (27%), 3,4-dibromo-2-methylthiophene (**2**) (24%), 4-bromo-2-methylthiophene (**3**) (5%), and 3-bromo-2-methylthiophene (**8**) (3%). Each of these products was identified by a comparison of its vpc retention time and spectral properties with those of authentic samples.[3]

4-Bromo-2-thiophenealdehyde Oxime (7).—The crude 4-bromo-2-thiophenealdehyde obtained from the reaction of 2.42 g (0.01 mol) of 2,4-dibromothiophene, 0.01 mol of BuLi in hexane, and 0.1 mol of DMF by the procedure of Gronowitz[4] was converted to 0.7 g (34%) of the oxime **7**: mp 150–151.5° (recrystallized from H_2O with the aid of Norit); ir 3200, 2870, 1645, 935, 900, 875, 830, 755 cm^{-1}.[11]

Anal. Calcd for C_5H_4BrNOS (**7**): C, 29.14; H, 1.96; N, 6.80. Found: C, 28.91; H, 1.90; N, 6.59.

2-Acetamidomethyl-4-bromothiophene (6).—A mixture of 0.21 g (0.001 mol) of **7**, 25 ml of ether, and 3 g (0.1 mol) of $LiAlH_4$ was heated under reflux for 2 hr. After destruction of the excess $LiAlH_4$ with wet ether the filtered solution was treated with 5 ml of acetic anhydride. Removal of the solvents on a rotary evaporator left a residue which was recrystallized from H_2O to give 0.11 g (47%) of **7**: mp 88.5–89°; nmr (CF_3COOH) τ 7.62 (s, 3, CH_3), 5.28 (d,[13] J = 5 Hz, 2, CH_2), 3.03 (m, 1, 5 H),[15] 2.86 (d, J = 1.8 Hz, 1, 3 H),[15] 1.50 (s, 1, NH); ir 3305, 1648, 1548, 825, 735 cm^{-1}.[11]

Anal. Calcd for C_7H_8BrNOS (**6**): C, 35.91; H, 3.44; N, 5.98. Found: C, 36.14; H, 3.60; N, 5.87.

Reaction of 3,4-Dibromo-2-methylthiophene (2) with Potassium Amide.—Following the previously described procedure,[3] 5.08 g (0.0197 mol) of **2** was treated with 0.039 mol of KNH_2 in liquid NH_3 at −33° for 15 min. The neutral fraction after work-up contained 2.8 g (55%) of recovered starting material, **2**, identified by its infrared spectrum. The acetylated basic fraction yielded 0.15 g (6%) of **6**, mp 88–89°, whose nmr and infrared spectrum were identical with those of authentic **6**.

Reaction of 4-Bromo-2-methylthiophene (3) with Potassium Amide.—One gram (0.00565 mol) of **3**[3] and 0.017 mol of KNH_2 were treated as above to give 0.85 g (85%) of recovered **3** in the neutral fraction. The acetylated basic fraction yielded a few milligrams of a white solid whose infrared spectrum was identical with that of **9** obtained as described below.

4-Acetamido-2-methylthiophene (9).—The acetylated basic fraction from the reaction of 2-bromo-5-methylthiophene (**10**) with potassium amide (reaction **1b** → **2b** in ref 3) contained a small amount (7%) of a tan, amorphous solid which after sublimation and crystallization from methanol–water gave white plates of **9**: mp 118–120°; nmr ($DCCl_3$) τ 7.90 (s, 3, CH_3CO), 7.60 (d, J = 1 Hz, 3, CH_3), 3.30 (m, 1, 5 H), 2.80 (d, J = 1 Hz, 1, 3 H); ir 3260, 1650, 820, 735 cm^{-1};[12] mass spectrum (70 eV) m/e (rel intensity) 155 (21), 113 (52), 112 (23), 80 (40), 45 (63), 43 (100), 39 (36), 28 (40), 15 (39).

Anal. Calcd for C_7H_9NOS (**9**): C, 54.16; H, 5.84; N, 9.03. Found: C, 54.38; H, 5.58; N, 8.82.

2-Bromo-5-methylthiophene (10).—To a solution of 7.3 g (0.075 mol) of 2-methylthiophene in 35 ml of dioxane was added 12 g (0.075 g-atom) of Br_2 in 75 ml of dioxane over a period of 1.5 hr. The reaction mixture was stirred at room temperature for an additional 5 hr and then treated with 400 ml of 10% $NaHCO_3$. The oily layer which separated was removed and the water layer was extracted with three 100-ml portions of ether. The combined oil and ether extracts were washed with two 50-ml portions of H_2O and dried (Na_2SO_4), and the ether was removed by distillation through a 40-cm Vigreux column. The residue was analyzed by vpc and the major product (84% yield) was identified as 2-bromo-5-methylthiophene (**10**), bp 68–69° (17 mm), by a comparison of its spectral properties with those of an authentic sample.[3,7]

Registry No.—**1**, 29421-73-6; **2**, 30319-01-8; **3**, 29421-92-9; **6**, 31767-00-7; **7**, 31767-01-8; **9**, 31767-02-9; **10**, 765-58-2; potassium amide, 17242-52-3.

Acknowledgment.—This research was generously supported by The Robert A. Welch Foundation and the Texas Christian University Research Foundation.

(10) P. Moses and S. Gronowitz, *Ark. Kemi*, **18**, 119 (1961).

(11) Although the region from 806–826 cm^{-1} is usually cited[12] as being characteristic of 2,4-disubstituted thiophenes, many such compounds also appear to have strong absorptions from 720 to 760 cm^{-1}.[1,3,12]

(12) S. Gronowitz, P. Moses, and A. Hornfeldt, *Ark. Kemi*, **71**, 237 (1961).

(13) This apparent doublet is also found in the nmr of the acetamide of the benzylamine (4.17 τ, J = 6 Hz in CCl_4) and is probably due to restricted rotation around the amide bond.[14]

(14) L. A. LaPlanche and M. T. Rogers, *J. Amer. Chem. Soc.*, **85**, 3728 (1963).

(15) A. R. Katritzky, "Physical Methods in Heterocyclic Chemistry," Vol. II, Academic Press, New York, N. Y., 1963, pp 117–121.

Boron Photochemistry. VIII. Oxidative Photocyclization of Anilinoboranes

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In a recent publication[1] we presented a novel photochemical synthetic route to the B-phenyl derivatives of

(1) P. J. Grisdale and J. L. R. Williams, *J. Org. Chem.*, **34**, 1675 (1969).

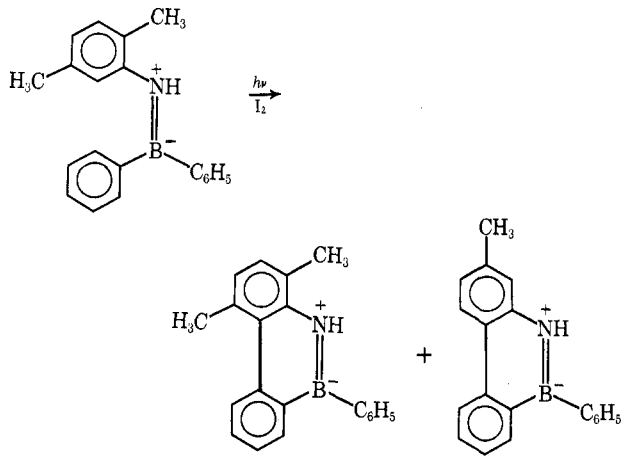
the borazaro-, boroxaro-, and borathiarophenanthrenes (**3**). The route for the photochemical and normal[2,3] syntheses of these heterocyclic phenanthrene systems is shown in Scheme I.

For simple unsubstituted boroxaro- and borazarophenanthrenes the photochemical route offers little advantage over the normal syntheses since the corresponding 2-hydroxy- and 2-aminobiphenyls (**4a**, **4b**) are readily available. For the borathiaro compound the photochemical route is preferable in that high yields of the desired compound **3c** are obtained. However, the great potential for the photochemical route to these systems is in its application to the synthesis of substituted derivatives. To date very few substituted derivatives of these systems have been reported, perhaps because of the experimental difficulties involved. As an example we can consider the borazarophenanthrene system. Two methods are available for the preparation of substituted derivatives: (a) electrophilic substitution in the nonheterocyclic rings[4,5] and (b) synthesis from a substituted 2-aminobiphenyl.[6] The former process yields a mixture of 6- and 8-substituted isomers together with some 6,8-disubstituted derivatives; the separation of these products is tedious and time-consuming. The latter process involves the synthesis of the corresponding substituted 2-aminobiphenyls which, in most cases, is very laborious. The photochemical approach outlined in Scheme II largely overcomes these problems.

The conversion of the R-substituted 2-iodoaniline (**5a**) to the R-substituted 10-phenyl-10,9-borazarophenanthrene (**7**) represents an extension of our previous findings. Since many 2-iodoanilines are easily prepared, this procedure offers an attractive route to the substituted heterocyclic compounds **7**. We have now discovered that the substituted anilines **5b**, when converted to the aminoboranes **6b**, can be oxidatively photocyclized in the presence of elemental iodine to furnish the derivatives **7** in moderate yield. This is analogous to the oxidative photocyclization of stilbene and other ethylenes,[7] but the ready availability of the aminoboranes **6b** makes this a very desirable procedure to obtain the borazarophenanthrene system substituted in the nitrogen-bearing ring.

Table I indicates the scope of the reaction. Included are yields determined from spectral data and of isolated analytical samples. The reaction can be applied to a large number of anilines substituted with either electron-donating or electron-withdrawing substituents. The reaction failed completely only in the case of *m*-nitro- and *p*-nitroanilines. The mass spectrum of the end product resulting from acetanilide indicated the presence of the unsubstituted compound which would result from aniline itself. This could result from deacetylation before or after the photocyclization step. Attempts to substitute strongly electron-withdrawing groups on nitrogen in borazarophenanthrenes have failed previously also.[8]

The position of a single substituent in the aniline has little effect on the yield. In the case of the meta-substituted anilines, two isomeric borazarophenanthrenes could be formed (the 5- and 7-substituted derivatives). We observed only one product in such cases, and steric effects would very much favor cyclization to yield the 7 isomer. In addition, we have good evidence from the cyclization of the dimethylanilines to indicate that this is so. Photocyclization of the aminoborane derived from 2,5-dimethylaniline and diphenylboron chloride yields a mixture of mono- and dimethyl heterocyclic compounds in approximately equal amounts. The



cleavage of a C–C bond leading to demethylation competes favorably with the formation of the sterically hindered 5,8-dimethyl derivative. In the case of 3,5-dimethylaniline we were unable to isolate a sample of the heterocycle for analysis, but mass spectral data on the crude mixture indicated the presence of the dimethylborazarophenanthrene. The positioning of a substituent in the 5 position is very unfavorable sterically, hence the reduced yield. The reaction involving 2,6-dimethylaniline yields the 8-methylborazarophenanthrene with elimination of a methyl group, although in this case there is no alternative route. Such eliminations have been observed in other oxidative photocyclization reactions.[9]

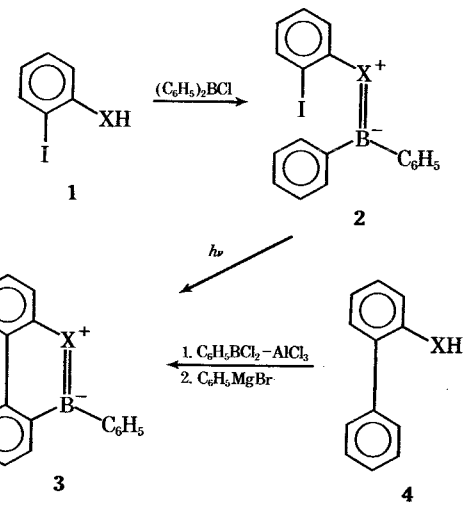
The *o*-bromoaniline also yields a mixture of borazarophenanthrenes, the unsubstituted derivative, and the 8-bromo compound. These probably result from competition between an oxidative photocyclization and one involving elimination of HBr, analogous to the case of *o*-iodoaniline.[1] In other radical reactions of halo-substituted benzenes, similar reactivity is observed for chloro, bromo, and iodo compounds.[10]

The amines which presented problems are listed in Table II with supporting data and comments.

All of the compounds listed in Table I had satisfactory mass spectral and nmr data. Their solutions all showed the typical ultraviolet spectrum of the borazarophenanthrene system with the two long-wavelength bands separated by about 15 nm. The majority had the long-wavelength band between 330 and 336 nm, but, for the 6-methoxy and 8-carbethoxy compounds, the band occurred at 345 and 347 nm, respectively.

(2) M. J. S. Dewar, V. P. Kubba and R. Pettit, *J. Chem. Soc.*, 3073 (1958).
(3) M. J. S. Dewar and V. P. Kubba, *J. Org. Chem.*, **25**, 1722 (1960).
(4) M. J. S. Dewar and V. P. Kubba, *Tetrahedron*, **7**, 213 (1959).
(5) M. J. S. Dewar and V. P. Kubba, *J. Org. Chem.*, **25**, 1722 (1960).
(6) M. J. S. Dewar and P. J. Grisdale, *ibid.*, **28**, 1759 (1963).
(7) E. V. Blackburn and C. J. Timmons, *Quart. Rev. (London)*, **23**, 482 (1969).
(8) M. J. S. Dewar and P. M. Maitlis, *Tetrahedron*, **15**, 35 (1961).
(9) K. L. Servis and K. N. Fang, *Tetrahedron Lett.*, No. 8, 967 (1968).
(10) J. T. Pinhey and R. D. G. Rigby, *ibid.*, **16**, 1267 (1969).

SCHEME I



SCHEME II

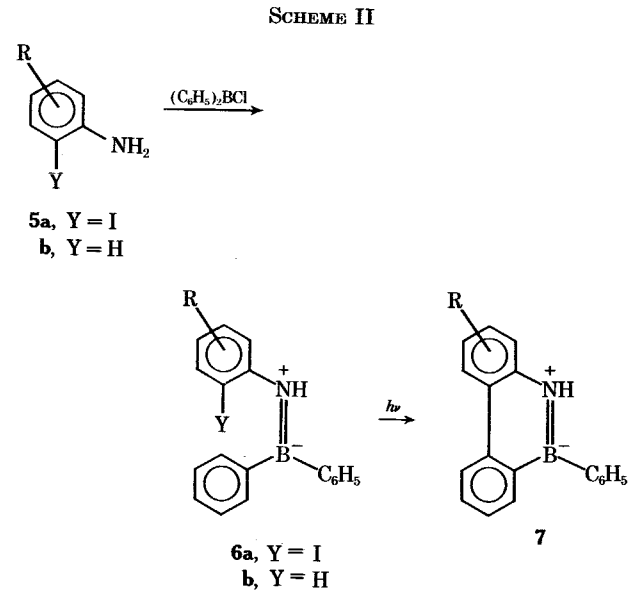
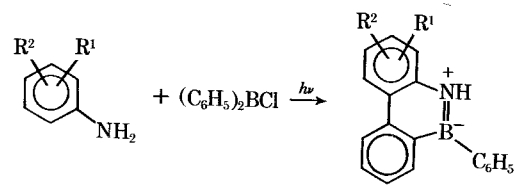


TABLE I.—DATA FOR THE SUBSTITUTED 10-PHENYL-10,9-BORAZAROPHENANTHRENES FROM THE REACTION



Substitution in aniline	Substitution in product	Registry no.	Yield, % (spectral)	Yield, % (isolated)	λ_{max}, nm	Mp, °C	Formula	Calcd, % C	H	B	N	Hal	Found, % C	H	B	N	Hal
2-Methoxy	8-Methoxy	31899-13-5	21	20	330	119–120	$C_{19}H_{16}BNO$	80.1	5.6	3.8	4.9		79.8	5.9	3.7	4.8	
3-Methoxy	7-Methoxy	31896-40-9	20	14	334	165–166	$C_{19}H_{16}BNO$						79.6	5.6	3.7	4.8	
4-Methoxy	6-Methoxy	31896-41-0	18	10	345	92–94	$C_{19}H_{16}BNO$						80.0	5.7	3.6	5.1	
2,3-Dimethyl	7,8-Dimethyl	31899-16-8	20	18	332	130–131	$C_{20}H_{18}BN$	84.9	6.3	3.8	4.9						
2,4-Dimethyl	6,8-Dimethyl	31899-17-9	29	27	336	136–138	$C_{20}H_{18}BN$						84.6	6.5	3.7	5.2	
N-Methyl	*N*-Methyl	31899-18-0	20	18	329	123–125	$C_{19}H_{16}BN$	84.8	6.0	4.0	5.2		84.5	6.1	3.9	5.1	
2-Methyl	8-Methyl	31899-19-1	55	33	331	94–96	$C_{19}H_{16}BN$						84.6	6.3	3.8	5.1	
3-Methyl	7-Methyl	31896-46-5	52	33	332	114–117	$C_{19}H_{16}BN$						84.6	6.3	3.8	4.8	
4-Methyl	6-Methyl	31899-20-4	38	30	337	117–119	$C_{19}H_{16}BN$						84.6	6.4	4.0	5.1	
None	None	19091-94-2	40	30	329	107–110	$C_{18}H_{14}BN$										
2-Chloro	8-Chloro	31896-49-8	29	20	329	109–111	$C_{18}H_{13}BClN$	74.7	4.5	3.7	4.8	12.3	74.8	4.7	3.6	5.0	11.8
3-Chloro	7-Chloro	31896-50-1	26	17	330	123–126	$C_{18}H_{13}BClN$						74.7	4.8		5.0	12.0
4-Chloro	6-Chloro	31896-51-2	29	15	336	104–106	$C_{18}H_{13}BClN$						74.5	4.8		4.9	12.3
4-Bromo	6-Bromo	31899-25-9		4	337	91–93	$C_{18}H_{13}BBrN$	64.7	3.9	3.2	4.2	23.9	64.9	3.1	3.1	4.4	23.9
2-Carbethoxy	8-Carbethoxy	31899-26-0		24	357	136–138	$C_{21}H_{18}BNO_2$	77.1	5.5	3.3	4.3		77.4	5.8	3.3	4.4	
4-Cyano	6-Cyano	31896-54-5	18	16	331	191–192	$C_{19}H_{13}BN_2$	81.5	4.6	3.9	10.0			5.0	3.9	9.6	

TABLE II
GLC/MASS SPECTRAL ANALYSES FOR PRODUCTS FROM THE PHOTOCYCLIZATION

Substitution in aniline	10-Phenyl-10,9-borazarophenanthrenes (*m/e* values)
N-Acetyl	Unsubstituted[a] (255)
2-Bromo	Unsubstituted[a] (255) + 8-bromo (333)
2,5-Dimethyl	7-Methyl[a] (269) + 5,8-dimethyl (283)
2,6-Dimethyl	8-Methyl[b,c] (269)
3,5-Dimethyl	5,7-Dimethyl (283)

[a] These compounds had identical uv spectra and glc retention times with those listed in Table I. [b] Reference 2. [c] This derivative was isolated in 35% yield, mp 94–96°.

The procedure described here provides a simple, novel route to substituted borazarophenanthrenes. In addition it may well prove convenient for the facile ortho phenylation of amines to yield various 2-aminobiphenyl derivatives, since the heterocyclic compounds readily deboronate in cold sulfuric acid.[3] As mentioned earlier, the synthesis of substituted 2-aminobiphenyls is a very laborious procedure. This type of synthesis also offers an attractive route to other condensed borazarohydrocarbons through suitable choice of diaryl boron halide and aromatic amine. These areas are under investigation and will be reported later.

Experimental Section

General.—All melting points are corrected. Spectra were determined with Cary Model 15 (uv) and Varian A-60 (nmr) instruments. Mass spectra were determined with a CEC 21-110B instrument, equipped with a heated inlet system as described by Caldecourt[11] but constructed of glass.

Analytical glpc was performed using an F & M Model 720 gas chromatograph equipped with a 0.25 in. × 10 ft column packed with 10% UCW 98 on Chromosorb W.

Materials.—Eastman grade amines were used without further purification but were thoroughly dried in the photoreactor. Chlorodiphenylborane was prepared by the method of Niedenzu, Beyer, and Dawson.[12]

Photocyclizations.—The horizontal thin-film photochemical reactor described earlier was used in these experiments.[13] A second side arm was added to facilitate the addition of solid elemental iodine to the reactor. The amines (10 mmol) were placed in the flask, which was then pumped out with gentle warming (infrared lamp) for 1 hr. It was filled with dry nitrogen and reevacuated, and the process was repeated. Finally 600 ml of dry cyclohexane was distilled off sodium hydride into the reactor. Chlorodiphenylborane (5 mmol) was then injected into the flask and the mixture was rotated for 0.5 hr at room temperature. Iodine (11 mmol) was introduced while a generous flow of dry nitrogen was passing through the flask. The solutions were irradiated using a Hanovia 100-W 608A-36 lamp in a quartz insert. The progress of the reaction was followed by withdrawing 100-μl samples, diluting them in methanol (3 ml) containing a trace of sodium sulfite, and examining the uv spectra. After 15–20 hr the concentration of the desired species usually reached a maximum and the cyclohexane solution was washed with three 200-ml portions of water, three 100-ml portions of dilute HCl, two 50-ml portions of sodium sulfite solution, three 100-ml portions of dilute sodium hydroxide solution, and finally two 100-ml portions of water. The cyclohexane was then dried and evaporated. The crude product was either passed through a short pad of silica and recrystallized from ligroin (bp 63–75°) or recrystallized immediately from ligroin (bp 63–75°). Physical data are listed in Table I.

(11) V. J. Caldecourt, *Anal. Chem.*, **27**, 1670 (1955).
(12) K. Niedenzu, H. Beyer, and J. W. Dawson, *Inorg. Chem.*, **1**, 738 (1962).
(13) J. L. R. Williams and P. J. Grisdale, *Chem. Ind. (London)*, 1477 (1968).

Synthesis of the Zinc(II) Chelate of 6-(α-Hydroxy-β-carbomethoxyethyl)pyrroporphyrin Methyl Ester

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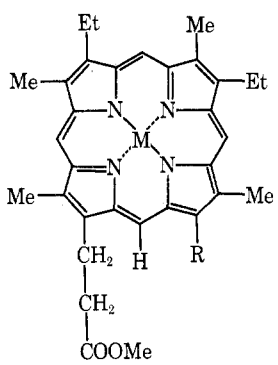
A porphyrin model compound with a β-ketopropionic acid side chain in the 6 position should be of interest since ring closure might take place between this side chain and the adjacent meso position forming a five-membered isocyclic ring. If such a ring closure takes place readily, a hypothesis concerning the biosynthesis of the isocyclic ring of the structurally similar chlorophyll may be advanced.

A β-hydroxypropionic acid derivative would be a convenient intermediate for this purpose and could be obtained from the corresponding formyl compound, using the Reformatsky reaction.

$$\text{porphyrin—CHO} + \text{BrCH}_2\text{COOCH}_3 + \text{Zn} \longrightarrow [\text{porphyrin—CH(OZnBr)CH}_2\text{COOCH}_3] \longrightarrow \text{porphyrin—CH(OH)CH}_2\text{COOCH}_3$$

Accordingly, 6-formylpyrroporphyrin methyl ester (**5**) was prepared from pheophytin (**1**). The conditions used were essentially those of Fischer[1] and Vida.[2] Compound **1** was degraded to pyrroporphyrin methyl ester (**2**). Compound **2** was converted to its Zn(II)



2, R = H; M = 2H
3, R = H; M = Zn
4, R = H; M = Fe
5, R = CHO; M = 2H
6, R = CHO; M = Zn
7, R = CH[OH]CH_2COOMe; M = Zn
8, R = CH=CHCOOMe; M = Zn

chelate **3** with zinc diacetate in acetic anhydride. Attempts to formylate the Zn(II) chelate were unsuccessful; therefore compound **3** was converted into the Fe(II) chelate **4** with ferrous acetate.

Compound **4** was formylated with dichloroethoxyethane in the presence of stannic chloride to yield the 6-formyl compound which in turn was converted to the Zn(II) chelate of 6-formylpyrroporphyrin methyl ester (**6**) with zinc diacetate.

In the Reformatsky reaction, compound **6** was treated with bromoacetic methyl ester to yield the Zn(II) chelate of 6-(α-hydroxy-β-carbomethoxyethyl)pyrropor-

(1) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Leipzig, 1937.
(2) J. Vida, Research Report, Harvard University, Cambridge, Mass., 1962.