loss of water already mentioned; (2) the ultraviolet spectrum shows $\lambda_{max}^{CHCl_3}$ 269 mμ (ε, 12000); (3) the infrared spectrum shows absorption at 5.52 μ (strained β-lactam), 5.9 μ (strained and conjugated γ-thiolactone), 6.0 μ (amide) and 6.1 μ (double bond); (4) the n.m.r. spectrum[11] shows absence of the tertiary hydrogen at carbon-3 and a doublet at $\tau = 7.83$ and 7.92 for the isopropylidene group; (5) ozonolysis affords acetone in excellent yield; no acetone is obtained upon ozonolysis of the parent penicillin.

The *anhydro*penicillins possess extraordinary chemical stability as compared with the parent penicillins. This is surprising in view of the highly strained bicyclic system of these compounds (see infrared data above). Thus they are recovered unchanged after prolonged refluxing in ethyl alcohol, aqueous dioxane or xylene. The *anhydro*penicillins display only weak antibacterial activity.[12] However, their increased chemical stability and the activation of the methyl groups by the adjacent double bond makes the introduction of substituents on the methyl groups possible by allylic attack. Some of the products thus obtained show antibacterial activity *and* stability to penicillinase. Details of these and related experiments will be reported in a subsequent paper.

Acknowledgments.—We thank Professor B. Belleau of the University of Ottawa for stimulating discussions which led to the correct structure, D. L. Evans for valuable assistance with the infrared spectra and Dr. L. C. Cheney for his advice and encouragement.

(11) Obtained in methylene chloride on the Varian A60 N.M.R. spectrometer. We thank D. L. Whitehead for this spectrum.

(12) Whereas penicillin G. shows a minimum inhibitory concentration *versus Staph. aureus Smith* of 0.02–0.05 γ/ml., *anhydro*benzylpenicillin inhibits growth at 70 γ/ml.

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SYNTHETIC PORPHYRINS RELATED TO CHLOROBIUM CHLOROPHYLLS

Sir:

Analytical evidence indicated that a tricarboxylic acid derived from fraction 5 of chlorobium phaeophorbide (660) degraded to a homolog of δ-phylloporphyrin wherein the distribution of methyl and ethyl groups on the 5- and δ-positions was uncertain.[1] This phylloporphyrin has since been isolated and characterized[2] as has a pyrroporphyrin[2] obtained in the same way from fraction 4 of chlorobium phaeophorbide (650).

We have synthesized the methyl ester of 1,3,8-trimethyl-2,4,5-triethylporphin-7-propionic acid (*Anal.* Calcd. for $C_{33}H_{38}O_2N_4$: C, 75.83; H, 7.33; N, 10.72. Found: C, 75.91; H, 7.48; N, 10.61) and of its δ-methyl derivative (*Anal.* Calcd. for $C_{34}H_{40}O_2N_4$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.27; H, 7.21; N, 10.61). These syntheses were analogous to a synthesis of pyrroporphyrin XV[3] and utilized the pyrromethenes from 2-formyl-3-bromo-4-ethyl-pyrrole-5-carboxylic acid with 2-methyl- or 2-ethyl-3-methyl-pyrrole-4-propionic acid.

The identity of the methyl ester of the above chlorobium pyrroporphyrin and the first synthetic porphyrin seemed assured but not clear-cut because of their polymorphism. Their copper complexes, however, showed identical m.p. (220–226°), mixed m.p. and X-ray powder photographs. This proved the 5-ethyl group in fraction 4 of chlorobium phaeophorbide (650), also proved by degradation to ethylmaleimide.[2] It also proved that the pairs of substituents have the hitherto assumed arrangements on the pyrrole rings as in phaeophorbide-a; this was also proved in the case of chlorobium phaeophorbide (650) fraction 6 by conversion to pyrophaeophorbide-a.[2]

The methyl ester of the above phylloporphyrin homolog from chlorobium and the second synthetic porphyrin were identical in m.p. (214–215.5°), mixed m.p., and in their exceptionally well defined X-ray powder photographs. A difficulty in the analytical evidence was resolved when it was found that our synthetic porphyrin, like the analytical one[1] but not as reported for δ-phylloporphyrin IV,[4] had bands II and III of its visible spectrum equal in intensity. The 5-ethyl group and the δ-methyl group, the preferred alternative on general grounds,[2] as well as the hitherto assumed arrangement of the substituents are thus proved in chlorobium phaeophorbide (660) fraction 5; the proton magnetic resonance data is consistent with a δ-alkyl group.[1]

We are also synthesizing porphyrins with the 4-*n*-propyl- and 4-isobutyl-substituents proved by the analytical work,[2] including 4-*n*-propyl-4-des-ethyl-des-oxo-phylloerytherin methyl ester, m.p. 236–238° (*Anal.* Calcd. for $C_{35}H_{40}O_2N_4$: C, 76.61; H, 7.35; N, 10.21. Found: C, 77.02; H, 7.15; N, 10.55), copper complex, m.p. 244–246° (*Anal.* Calcd. for $C_{35}H_{38}O_2N_4$: C, 68.90; H, 6.28; CuO, 12.39. Found: C, 68.56; H, 6.34; residue, 12.39). This awaits analytical material for comparison.

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(1) A. S. Holt, D. W. Hughes, H. J. Kende and J. W. Purdie, *J. Am. Chem. Soc.*, **84**, 2835 (1962).

(2) A. S. Holt and J. W. Purdie, in preparation.

(3) H. Fischer, H. Berg and A. Schormüller, *Ann.*, **480**, 144 (1930).

(4) H. Fischer and H. Orth, "Chemie des Pyrrols," II/1, Leipzig, 1937, p. 360.

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INTRINSIC COTTON EFFECTS IN COLLAGEN AND POLY-L-PROLINE[1,2]

Sir:

Previous investigations of collagen solutions have shown that the optical rotation in the visible and near ultraviolet regions undergoes large changes from highly negative to less negative values upon denaturation.[3] Rotatory dispersion measurements, in spectral regions removed from absorption bands, on both native and denatured collagen solutions fit the one-term Drude equation as do dispersion data from random coil polypeptides and proteins with low helix contents.[4] Recently, acceptable models for the molecular structure of collagen have been proposed[5,6] which involve three left-handed polyglycine-poly-L-proline II type helices wound in a right-handed super helix. In this com-

(1) This is Polypeptides XLII. For the preceding paper in this series see reference 16.

(2) This work was supported in part by U. S. Public Health Service Grant A2558 and in part by the Office of the Surgeon General, Department of the Army.

(3) See for example: C. Cohen, *J. Biophys. and Biochem. Cytology*, **1**, 203 (1955).

(4) For reviews on rotatory dispersion measurements see: (a) E. R. Blout, Chapter 17 in "Optical Rotatory Dispersion" by C. Dierassi, McGraw-Hill Book Company, New York, N. Y., 1960; (b) P. Urnes and P. Doty in "Advances in Protein Chemistry," Vol. 16, C. B. Anfinsen, N. L. Anson, K. Bailey and J. T. Edsall, editors, Academic Press, Inc., New York, N. Y., 1961, p. 401.

(5) (a) G. N. Ramachandran and G. Kartha, *Nature*, **174**, 269 (1954); (b) **176**, 593 (1955).

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