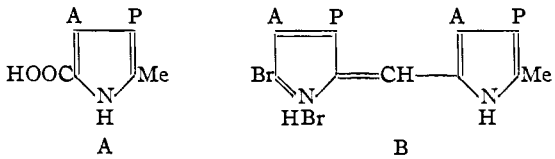
252–253°. This m.p. was not depressed by an authentic synthetic specimen, and the identity was confirmed by solubility, crystal form, visible and infrared spectra.



A = $CH_2 \cdot COOH$
P = $CH_2CH_2 \cdot COOH$

The m.p. of the synthetic porphin-1,3,5,7-tetraacetic acid-2,4,6,8-tetrapropionic acid octamethyl ester was not depressed by the purest uroporphyrin I methyl ester,[6] and their identity was confirmed by comparison of their visible spectra, infrared spectra, and X-ray powder photographs.

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(6) C. Rimington and P. A. Miles, *Biochem. J. (London)*, **50**, 202 (1951).

(7) National Research Council of Canada Postdoctoral Fellow.

A METHOD FOR THE SYNTHESIS OF CYCLIC POLYPEPTIDES

Sir:

The recognition of the cyclic nature of several of the antibiotic polypeptides has focused attention on the paucity of methods for the synthesis of cyclic peptides with rings larger than those of diketopiperazines. It is the purpose of this communication to report a procedure for the synthesis of such "cyclopeptides" by the catalytic hydrogenolysis of carbobenzoxypeptide azides. The method is exemplified by the synthesis of cyclo-DL-phenylalanylglycylglycine.

Carbobenzoxy-DL-phenylalanylglycylglycine hydrazide, m.p., 170–171° (*Anal.* Calcd. for $C_{21}H_{25}O_5N_5$: N, 16.4. Found: N, 16.0 (Dumas)), was converted to the azide in the usual manner. A solution of the azide (from 0.54 g. of the hydrazide) in 500 ml. of dry ethyl acetate was introduced slowly (at room temperature over a period of 26 hours) into 750 ml. of dry ethyl acetate containing *ca.* 2 g. of palladium black,[1] hydrogen being bubbled through the solution After 29 hours, the catalyst was removed by filtration, the solution was allowed to stand at room temperature overnight, and it was then concentrated *in vacuo* to a small volume. The resulting solid product was collected, washed with ethyl acetate, and reprecipitated from ethanol with ether; yield, 0.1 g. The cyclic tripeptide decomposed at 177–179° (*Anal.* Calcd. for $C_{13}H_{15}O_3N_3$: C, 59.8; H, 5.8; N, 16.1. Found: C, 60.0; H, 6.0; N, 15.6 (Dumas)). A determination of the molecular weight by the method of Cottrell[2] gave a value of 250, as compared with the theoretical value of 261. The Van Slyke nitrous acid method gave a value of 0.045 per cent. NH_2-N, indicating the absence of free amino groups. The product gave no color with ninhydrin (3 mg. heated with 2 ml. of 0.25 per cent. solution in 1:1 pyridine–water). Hydrolysis with 6 *N* hydrochloric acid at 100° for 24 hours, followed by chromatographic examination of the hydrolysate, gave a molar ratio of glycine to phenylalanine of 1.9:1. The cyclic peptide is soluble in methanol, ethanol, glacial acetic acid, and hot water; it is sparingly soluble in ethyl acetate, ether, cold water, or aqueous acid or alkali. When a suspension of the product in aqueous picric acid-sodium carbonate is heated, a permanent orange-red color is produced. 2,5-Diketopiperazine also gives a positive reaction,[3] but the color fades on standing. The infrared spectrum of the cyclic tripeptide differs from that of glycycl-L-phenylalanine anhydride.

While this work was in progress, the report of Boissonas and Schuman[4] appeared on the preparation of a cyclic peptide from D-leucylglycylglycine by treatment with ethyl chloroformate in dimethylformamide; no quantitative analytical data were presented, however, to establish the identity of the product with the desired cyclopeptide.

(1) C. A. Dekker and J. S. Fruton, *Methods in Medical Research*, **3**, 280 (1950).

(2) F. G. Cottrell, THIS JOURNAL, **41**, 721 (1919).

(3) E. Abderhalden and E. Komm, *Z. physiol. Chem.*, **139**, 181 (1924).

(4) R. A. Boissonas and I. Schuman, *Helv. Chim. Acta*, **35**, 2229 (1952).

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EVIDENCE FOR COBALT HYDROCARBONYL AS THE HYDROFORMYLATION CATALYST

Sir:

It has been postulated[1] and indirect evidence has been presented[2,3] that cobalt hydrocarbonyl, a strong acid, is the catalyst for the reactions that occur under hydroformylation conditions (90–200° and 100–300 atmospheres of synthesis gas (mixtures of hydrogen and carbon monoxide) in the presence of cobalt). However, the presence of the hydrocarbonyl, $HCo(CO)_4$, during or after the reaction has been difficult to demonstrate. This communication presents experimental work which shows that (a) cobalt hydrocarbonyl is formed under hydroformylation conditions, and (b) pure hydrocarbonyl in the absence of carbon monoxide and hydrogen reacts with certain substrates at room temperature and 1 atmosphere to give products that are also secured from the same substrates under hydroformylation conditions.

(a) Treatment of a solution of dicobalt octacarbonyl in pyridine with synthesis gas at 120° and 230 atmospheres resulted in the conversion of all of the cobalt to the pyridinium salt of cobalt hydrocarbonyl, $[C_5H_5NH]^+[Co(CO)_4]^-$. The same salt was obtained by adding pure cobalt hydrocarbonyl to pyridine at room temperature.

(b) The products from experiments involving

(1) (a) O. Roelen, Office of Tech. Services, U. S. Dept. Commerce, PB 81383; (b) H. Adkins and G. Krsek, THIS JOURNAL, **70**, 383 (1948); (c) I. Wender and M. Orchin, U. S. Bureau of Mines Rep. of Investigations 4270 (1948).

(2) I. Wender, S. Metlin and M. Orchin, THIS JOURNAL, **73**, 5704 (1951).

(3) I. Wender, H. Greenfield, S. Metlin and M. Orchin, *ibid.*, **74**, 4079 (1952).