following manner. A 5.3-g. sample, m.p. 156–163°, was treated with a mixture of 15 cc. of carbon disulfide and 5 cc. of nitromethane, whereupon all but 1.92 g. of solid dissolved. The insoluble portion was crystallized twice from acetone to yield 0.70 g. of **2,2,5,5-tetraphenyltetrahydrofuran** (I). Recrystallizations of the soluble portion of the original mixture eventually yielded 0.12 g. of **1,1,4,4-tetraphenyl-1,3-butadiene** (III) as the only other compound which could be isolated in pure condition.

DEPARTMENT OF CHEMISTRY
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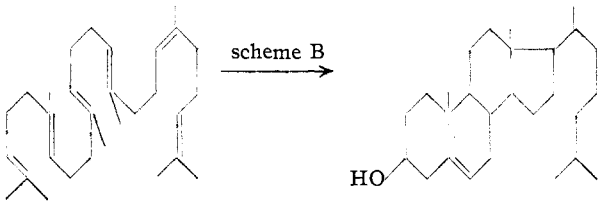
LOS ANGELES, CALIFORNIA

COMMUNICATIONS TO THE EDITOR

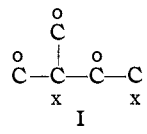
ON THE INCORPORATION OF ACETATE INTO CHOLESTEROL

Sir:

It has recently been demonstrated[1] that squalene is an efficient precursor of cholesterol and is most likely an intermediate in the conversion of acetate to this sterol. A pathway by which this hydrocarbon could be transformed into cholesterol was suggested by Robinson[2] in 1934 (route A). The recent findings[3,4] that the sterols and tetracyclic triterpenes are most likely of the same absolute configuration have suggested an alternate mechanism for the utilization of squalene in the biosynthesis of cholesterol (scheme B).



Degradation of the side-chain[5] and of ring A[6] of cholesterol formed from C^{14}-labeled acetate in biological experiments has indicated that such a biosynthesis might proceed by condensation of isoprenoid units labeled as shown in (I).[7] Therefore, if route A was followed



I

carbon atoms 10, 13, 20 and 25 of cholesterol would be derived from a carboxyl carbon of acetate and carbon atoms 18, 19, 21 and 26 from the methyl carbon. Such would not be the case if the tetracyclic triterpenoid type of scheme (B) was followed since a migration of a carbon atom would be involved. Thus in route B, carbon atoms 10, 20 and 25 would be from carboxyl carbons and carbon atoms 13, 18, 19, 21 and 26 from methyl carbons. Hence, the acetic acid derived from a Kuhn–Roth oxidation of cholesterol which had been formed biosynthetically from C^{14}-methyl-labeled acetic acid should contain C^{14} in the carboxyl group if route B was followed and not if route A was utilized.

Such an experiment was performed and the acetic acid so obtained was degraded by a Schmidt reaction. It was found that the acetic acid had a specific activity of 55,[8] the carboxyl carbon had 35 and the methyl carbon had 74. It is seen that the carboxyl carbon atom of acetic acid derived from cholesterol possessed C^{14} as would be predicted by route B and thus would rule against the Robinson postulate (route A).

If one assumes that the ratio of methyl carbons to carboxyl carbons in cholesterol derived from acetate[9] is 15/12 and that 5 of the 8 carbon atoms of the 4 molecules of acetic acid (from the angular positions as discussed above) obtained from the Kuhn–Roth oxidation of such a labeled cholesterol are, in turn, derived from the methyl carbons, then the specific activity of the carbon dioxide obtained by decarboxylation of acetic acid should have a value of only 22. The higher value, 35, can be reconciled by consideration of the involvement of the progenitor, methyl-labeled acetate, in the tricarboxylic acid cycle which would lead to some doubly-labeled acetate. This degree of randomization is of the same order of magnitude as recently reported by Cornforth, Hunter and Popják.[6]

These results strongly indicate that if squalene is directly utilized in the synthesis of cholesterol, a reaction scheme of type B is strongly suggested.[10]

(1) R. G. Langdon and K. Bloch, *J. Biol. Chem.*, **200**, 135 (1953).
(2) R. Robinson, *J. Soc. Chem. Ind.*, **53**, 1062 (1934).
(3) W. Klyne, *J. Chem. Soc.*, 2916 (1952).
(4) W. G. Dauben, D. F. Dickel, O. Jeger and V. Prelog, *Helv. Chim. Acta*, **36**, 325 (1953).
(5) J. Wüersch, R. L. Huang and K. Bloch, *J. Biol. Chem.*, **195**, 439 (1952).
(6) J. W. Cornforth, G. D. Hunter and G. Popják, *Biochem. J.*, **53**, xxiv (1953).
(7) The methyl carbon of acetate is denoted by o and the carboxyl carbon by x.
(8) All specific activities are expressed as dis./min./mg. $BaCO_3$
(9) H. N. Little and K. Bloch, *J. Biol. Chem.*, **183**, 33 (1950).
(10) A recent report by Woodward and Bloch (THIS JOURNAL, **75**, 2023 (1953)) has suggested the same reaction scheme.

DEPT. OF CHEMISTRY AND — W. G. DAUBEN
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RECEIVED MAY 1, 1953

POSSIBLE SIGNIFICANCE OF LACTONES AS INTERMEDIATES IN OXIDATION OF CARBONACEOUS MATERIALS

Sir:

Controlled oxidation of aqueous, alkaline suspensions of bituminous coals results in the conversion of about 50% of the carbon to a mixture of

water-soluble, polycarboxylic acids.[1] Recent studies in this Laboratory of the reaction products from decarboxylation of the copper salts of these acids have resulted in the recovery of the lactone of 2'-hydroxy-2-biphenylcarboxylic acid (6-dibenzopyrone), along with mono- and bicyclic aromatic hydrocarbons. This lactone was characterized by melting point, ultimate analysis, and comparison of infrared spectrum, of ultraviolet spectrum, and of properties of the methoxy acid derivative with those of an authentic sample.

The isolation of this lactone from the oxidation products of coal is highly suggestive in connection with oxidation mechanisms of carbonaceous materials. Lactone rings are very sensitive to *p*H. In an alkaline hydroxide solution, the ring is opened and the resultant hydroxyl and carboxyl groups will undergo the usual reactions of such groups. In an acid medium, a stable six-membered oxygen-containing ring is formed and further attack on interior rings would be expected to be difficult. The presence of lactones as intermediates would furnish a possible explanation for the much higher rates of oxidation of coals in alkaline than in acid media. Nitric acid is a very effective reagent in the primary stages of the oxidation of coals and various forms of carbon, but to complete the oxidation to benzenecarboxylic acids it has been found advantageous to follow the primary nitric acid oxidation with a secondary one in alkaline medium.[2] The formation of stable lactone rings in the acidic stage would account for such behavior. This lactone of the biphenyl hydroxy acid is relatively insoluble in aqueous sodium carbonate and this fact suggests an explanation for the lower oxidation rates of coal in sodium carbonate compared with sodium hydroxide solutions. The highest methoxyl values for "regenerated humic acids" are obtained by the Waliaschko[3] method, where the compound is dissolved in an excess of alcoholic potash before reaction with dimethyl sulfate. One would expect very complete opening of lactone rings under such circumstances. The esters of acids from oxidation of coal have been shown to form adducts with stannic chloride in dilute pentane solutions. This lactone forms such an adduct under identical experimental conditions.

It has been reported[4] that the rate of reaction of ozone on coal is markedly affected by the presence of water and that the action of this oxidizing agent on "regenerated humic acids" is greatly accelerated if the acids have been previously treated with boiling aqueous alkali. These facts point to a hydrolytic step in the reaction mechanism.

It is well established that the reaction of steam or water with carbon is greatly accelerated by the presence of alkalies; the opening of peripheral lactone rings could be responsible for the effect. It is possible that surface oxygen complexes, such as the C_xO_y of Rhead and Wheeler,[5] consist in part of lactone rings in peripheral positions. That such lactones can be produced by gas phase oxidation has been demonstrated recently by Brooks[6] who obtained this identical lactone by the air oxidation of phenanthrene in a fluidized catalyst bed at 370°.

(1) N. W. Franke, M. W. Kiebler, C. H. Ruof, T. R. Savich and H. C. Howard, *Ind. Eng. Chem.*, **44**, 2784–2792 (1952).

(2) B. Juettner, THIS JOURNAL, **59**, 208–213 (1937); O. Grosskinsky, *Glückauf*, **86**, 988–995 (1950).

(3) N. Waliaschko, *Arch. Pharm.*, **242**, 242 (1904).

(4) C. R. Kinney and L. D. Friedman, THIS JOURNAL, **74**, 57–61 (1952).

(5) T. F. E. Rhead and R. V. Wheeler, *J. Chem. Soc.*, **101**, 846 (1912); **103**, 461 (1913).

(6) J. D. Brooks, *Research*, **5**, 196 (1952).

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RECEIVED MAY 16, 1953

REACTIONS OF ALLYL ALCOHOL-1-C^{14}

Sir:

Although an allylic rearrangement would be expected to occur when allyl alcohol is transformed into an allyl halide under certain experimental conditions, the extent to which it takes place has not been determined. In the present work allyl alcohol-1-C^{14} was converted to radioactive allyl chloride and allyl bromide by different methods, the starting material and final products degraded with ozone, and the amount of rearrangement determined from the specific activity of the formaldehyde-C^{14}.

By modification of the excellent method of Young and Lane[1] carbon-14 labeled allyl bromide was prepared from allyl alcohol-1-C^{14}, phosphorus tribromide, and pyridine at −80°. Upon degradation with ozone, the per cent. rearrangement to allyl bromide-3-C^{14} was found to be 46%.

Radioactive allyl chloride was made from allyl alcohol-1-C^{14} and thionyl chloride by the method of Meisenheimer and Link[2] and the amount of rearrangement to allyl chloride-3-C^{14} was 51%.

Finally, the tosylate of allyl alcohol-1-C^{14} was treated with sodium bromide in a suitable solvent and only allyl bromide-1-C^{14} resulted indicating no rearrangement.

Further study is in progress with allyl alcohol-1-C^{14} and allyl bromide-1-C^{14} to determine if in those cases where rearrangement occurs a unimolecular process of replacement involving the formation of a resonating cation is the predominant mechanism.

(1) W. G. Young and J. F. Lane, THIS JOURNAL, **59**, 2051 (1937).

(2) J. Meisenheimer and J. Link, *Ann.*, **479**, 211 (1930).

DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING
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URBANA, ILLINOIS JOHN C. LEAK

RECEIVED MAY 11, 1953

ENZYMATIC SYNTHESIS OF D-GLUTAMINE AND RELATED HYDROXAMIC ACIDS

Sir:

The mechanism of the enzymatic interaction of ATP,[1] L-glutamate, and ammonia, yielding ADP, L-glutamine, and inorganic phosphate has been of interest since the reaction was first described by Speck[2] and by Elliott.[3] Elliott,[4] using a highly purified enzyme from peas, was unable to separate glutamine synthesis from glutamotransferase ac-

(1) Abbreviations employed: ATP = adenosine triphosphate, ADP = adenosine diphosphate, tris = tris-(hydroxymethyl)-aminomethane.

(2) J. F. Speck, *J. Biol. Chem.*, **168**, 403 (1947); **179**, 1387, 1405 (1949).

(3) W. H. Elliott, *Nature*, **161**, 128 (1948).

(4) W. H. Elliott, *J. Biol. Chem.*, **201**, 661 (1953).

tivity.[5,6] Although it appears that glutamine synthesis probably occurs by a stepwise reaction, there is no clear evidence for an intermediate. Recently, Black and Gray[7] reported evidence for β-L-aspartyl phosphate as the product of the enzymatic reaction of L-aspartate and ATP, a finding which renews interest in the possibility of a similar intermediate in glutamine synthesis.

We now report the enzymatic synthesis of hydroxamic acids from D-glutamate, and from both isomers of α-aminoadipate, using the enzyme obtained from peas,[4] as well as enzymes from pigeon liver[2] and sheep brain.[3] When ammonia was substituted for hydroxylamine, D-glutamine was formed, but at less than half the rate observed for D-glutamohydroxamic formation. There was no detectable amide formation from α-aminoadipate under the conditions employed (Table I).

TABLE I

Units—μM formed/mg. enzyme N. Digests contained 50 μM $MgCl_2$, 100 μM neutralized hydroxylamine hydrochloride or NH_4Cl, 50 μM glutamic acid or α-aminoadipic acid neutralized with tris, 25 μM β-mercaptoethanol, 10 μM sodium ATP, 50 μM imidazole buffer, *p*H 7.0. Incubated at 37° for 15 to 40 minutes, with sufficient pea enzyme to effect the synthesis of 2 to 4 μM of hydroxamic acid or amide with active substrates. Final volume, 1.0 ml.; *p*H 7.0. Values corrected by subtraction of blanks. The isomers of aspartic acid are not appreciably active in this system.

Substrate	Hydroxamic acid formed[8] (units/hour)	Amide formed, expressed as phosphate liberated[9] (units/hour)
L-Glutamate	407	428
D-Glutamate	385	171
L-α-Aminoadipate	19.8	0
D-α-Aminoadipate	24.6	0

The D-glutamate[10] employed in these experiments was obtained from the racemate by enzymatic resolution[11] or by the action of *Cl. welchii* decarboxylase.[12] The D-glutamine formed enzymatically was isolated in crystalline form ($[\alpha]^{26}D$ −6.5°), and was identified by paper chromatography, and by its failure to yield carbon dioxide with *Cl. welchii* decarboxylase. Both isomers of glutamine are deamidated by this preparation, but only L-glutamine yields carbon dioxide.

The fact that hydroxamic acids are formed from L- and D-glutamate at similar rates, while D-glutamine is formed considerably less rapidly, suggests the possibility of an initial activation of the glutamate which is of low optical specificity, followed by a more specific reaction with ammonia which becomes rate limiting in the case of D-glutamate. Such a limitation is not noted with hydroxylamine, which is known to react non-enzymatically with acyl phosphates, thiolesters, and certain other compounds. The apparent failure to synthesize the amides of the α-aminoadipate isomers is compatible with the view that the reaction of ammonia with an intermediate is relatively specific. On the other hand, racemic α-methylglutamic acid reacts in this system with both hydroxylamine and ammonia.[13,14]

It is of interest that study of the transferase reaction indicates a high degree of specificity (Table II).

TABLE II

For units, see Table I. Digests contained 50 μM $MgCl_2$, 1 μM sodium ADP, 50 μM glutamine or α-aminoadipamic acid, 100 μM neutralized hydroxylamine hydrochloride, 20 μM β-mercaptoethanol, 5 μM phosphate buffer *p*H 6.6. Incubated at 37° for 15 to 30 minutes, with sufficient pea enzyme to effect the formation of 0.5 to 1.0 μM of hydroxamic acid. Final volume, 1.0 ml.; *p*H 6.5. Values corrected by subtraction of blanks.

Substrate	Hydroxamic acid formed[8] (units/hour)
L-Glutamine	286
D-Glutamine[15]	3.93
L-α-Aminoadipamic acid[15]	0

While these findings might be interpreted as indirect evidence for an intermediate acyl phosphate similar to that described by Black and Gray,[7] we have been unable to obtain any evidence for a free phosphorylated product of the reaction of ATP and the glutamate or aminoadipate isomers.

The authors wish to thank Dr. Jesse P. Greenstein for generous samples of the isomers of glutamic and α-aminoadipic[16] acids.

(5) P. K. Stumpf and W. D. Loomis, *Arch. Biochem.*, **25**, 451 (1950).

(6) M. Schou, N. Grossowicz, A. Lajtha and H. Waelsch, *Nature*, **167**, 891 (1951).

(7) S. Black and N. Gray, THIS JOURNAL, in press. We thank the authors for making a copy of this paper available to us prior to publication.

(8) F. Lipmann and L. C. Tuttle, *J. Biol. Chem.*, **159**, 21 (1945).

(9) C. H. Fiske and Y. SubbaRow, *ibid.*, **66**, 375 (1925).

(10) The D-glutamate and D-glutamine employed contained less than 0.1% of their respective enantiomorphs, *cf.* A. Meister, L. Levintow, R. B. Kingsley, and J. P. Greenstein, *ibid.*, **192**, 535 (1951).

(11) V. E. Price, J. B. Gilbert, and J. P. Greenstein, *ibid.*, **179**, 1169 (1949).

(12) M. M. Camien, L. E. McClure and M. S. Dunn, *Arch. Biochem.*, **28**, 220 (1950).

(13) B. M. Braganca, J. H. Quastel and R. Schucher, *Arch. Biochem. and Biophys.*, **41**, 478 (1952).

(14) N. Lichtenstein, H. E. Ross and P. P. Cohen, *Nature*, **171**, 45 (1953); *J. Biol. Chem.*, **201**, 117 (1953).

(15) Preparation and properties to be reported.

(16) J. P. Greenstein, S. M. Birnbaum and M. C. Otey, THIS JOURNAL, **75**, 1994 (1953).

NATIONAL CANCER INSTITUTE
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RECEIVED MAY 16, 1953

THE SYNTHESIS OF UROPORPHYRIN I

Sir:

The structure proposed for uroporphyrin I by Hans Fischer[1] has been confirmed by synthesis.

The Pyrrole A[2] was brominated to give the crystalline methene B which, when fused with methylsuccinic acid for six hours at 118° cf [3], gave porphin-1,3,5,7-tetraacetic acid-2,4,6,8-tetrapropionic acid as the octamethyl ester m.p. 290–292°[4] (5.7%). Analysis gave no indication of partial decarboxylation [Calcd. for $C_{48}H_{54}O_{16}N_4$: C, 61.14; H, 5.77; N, 5.94; OCH_3, 26.33; C–CH_3, 0.0. Found: C, 61.00; H, 5.85; N, 5.76; OCH_3, 26.38; C-CH_3, 0.0.] In analogous cases, this method has given type I porphyrins exclusively. Here, the type was confirmed by partial decarboxylation to coproporphyrin I[5] obtained as the tetramethyl ester m.p.

(1) H. Fischer and H. Orth, "Chemie des Pyrrols," Akademische Verlag, Leipzig, 1937, Band II/I, p. 504 ff.

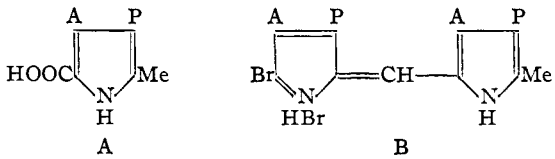
(2) S. F. MacDonald, *J. Chem. Soc.*, 4184 (1952).

(3) H. Fischer and H. Zischler, *Z. physiol. Chem.*, **245**, 123 (1937).

(4) M.p.s. (hot stage) are corrected.

(5) H. Fischer and W. Zerweck, *Z. physiol. Chem.*, **137**, 242 (1924).

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.

DIVISION OF PURE CHEMISTRY
THE NATIONAL RESEARCH COUNCIL S. F. MACDONALD
OTTAWA, CANADA R. J. STEDMAN[7]

RECEIVED MAY 21, 1953

(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).

DEPARTMENT OF BIOCHEMISTRY
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RECEIVED MAY 7, 1953

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).

treatment of selected substrates with cobalt hydrocarbonyl at atmospheric pressure are compared in Table I with the products secured by reaction of the same substrates under hydroformylation conditions. The experiment at atmospheric pressure with cyclohexene is typical: Cobalt hydrocarbonyl (4.0 g., 0.023 mole) was collected in a liquid-nitrogen trap containing 7.0 g. (0.085 mole) of cyclohexene. On warming, the cobalt hydrocarbonyl dissolved in the olefin without noticeable decomposition. At about 15°, the solution began to darken, a small amount of gas was given off, and a noticeable amount of heat was evolved. Upon addition of 2,4-dinitrophenylhydrazine, the 2,4-dinitrophenylhydrazone of cyclohexanecarboxaldehyde was obtained from the reaction mixture; it melted at 167.5–168.3°[4] after one recrystallization from ethanol. The yield of cyclohexanecarboxaldehyde, determined from the weight of hydrazone obtained, was 16 per cent., based on cobalt hydrocarbonyl added.

Further, it has now been found that bases suppress the hydroformylation reaction. Thus, the hydroformylation of a mixture of 2,3-dimethylbutene-1 and -2 at 135° and 230 atmospheres of synthesis gas was completely inhibited in the presence of triethylamine. The hydrogenation of benzhydrol, which proceeds readily under the usual hydroformylation conditions,[5] failed to occur when pyridine was used as a solvent.

These results strongly support the hypothesis that cobalt hydrocarbonyl catalyzes the variety of reactions that occur under hydroformylation conditions.

TABLE I

PRODUCTS SECURED FROM VARIOUS SUBSTRATES BY HYDROFORMYLATION AND BY REACTION WITH COBALT HYDROCARBONYL

Substrate	Products: Hydroformylation conditions	Products: Cobalt hydrocarbonyl
Cyclohexene	Cyclohexanecarboxaldehyde[a]	Cyclohexanecarboxaldehyde[b]
Hexene-1 (excess)	Heptaldehyde[c]	C_7 aldehydes[d]
	2-Methylhexanal[c]	
	Hexene-2[d]	Hexene-2[d]
	Hexene-3[d]	Hexene-3[d]
	No hexene-1[d]	No hexene-1[d]
α-Methylstyrene	Isopropylbenzene[e]	Isopropylbenzene[f]
	3-Phenylbutyraldehyde[g]	C_{10} aldehyde[d,f]
Benzyl alcohol	Toluene[h]	Toluene[f]
	2-Phenylethanol[h]	
Benzhydrol	Diphenylmethane[h]	Diphenylmethane[d,i]
Triphenylcarbinol	Triphenylmethane[h]	Triphenylmethane[j]

[a] 35% yield. 2,4-Dinitrophenylhydrazone, m.p. 167.5–168.5°; see reference 4. [b] 16% yield. 2,4-Dinitrophenylhydrazone, m.p. 167.5–168.3°; a mixed melting point of the hydrazones from both sources gave no depression. [c] H. Adkins and G. Krsek, THIS JOURNAL, 71, 3051 (1949). [d] Identified by infrared analysis. We wish to thank Dr. R. A. Friedel for the spectra determinations. [e] 69% yield; $n^{25}D$ 1.4910. [f] Identified by mass spectrometric analysis. [g] 9% yield. The aldehyde was reduced to the corresponding alcohol; the infrared spectrum of this alcohol was identical with that of an authentic sample. [h] See ref. 5. [i] Reaction run in acetone. Product isolated by chromatographic adsorption on alumina in 33% yield; benzophenone (12%) was present. [j] Reaction run in acetone. Product obtained in 95% yield, m.p. 92–93°, not depressed when mixed with an authentic sample.

(4) G. Natta, P. Pino and E. Mantica, *Gazz. chim. ital.*, **80**, 680 (1950).

(5) I. Wender, H. Greenfield and M. Orchin, THIS JOURNAL, **73**, 2656 (1951).

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RECEIVED APRIL 14, 1953

SYNTHESIS OF A REVERSIBLY CONTRACTILE AMPHOTERIC POLYPEPTIDE

Sir:

K. H. Meyer[1] has suggested that the contraction and relaxation of muscle may be attributed to the electrostatic attraction and repulsion of the ionized ammonium and/or carboxyl groups in the molecule of myosin. Recently Kuhn, Katchalski and their collaborators[2–6] have synthesized such mechanochemical systems composed of vinyl-type polyanions. Such systems are, of course, very useful and instructive, but the polypeptide-type polyampholyte is more desirable. We have now synthesized a three-dimensional amphoteric polypeptide network, composed of L-glutamic acid, L-lysine and DL-cystine residues and realized its reversible contraction and extension.

A mixture of anhydro-α-N-carboxy-ε-N-carbobenzoxy-L-lysine (8 millimoles), anhydro-α-N-carboxy-γ-benzyl L-glutamate (8 millimoles) and bis-(anhydro-N-carboxy)-DL-cystine (0.4 millimole) was dissolved in dry chlorobenzene–pyridine mixture and polymerized. After being precipitated with petroleum ether, the polymer was obtained quantitatively as a white powder. *Anal.* Calcd. for $[(C_{12}H_{13}NO_3)_{20}(C_{14}H_{18}N_2O_3)_{20}(C_6H_8N_2O_2S_2)_1]_n$: N, 8.8. Found: N, 8.7.

The reduction of this polymer by phosphonium iodide gave the hydriodide of a linear polypeptide consisting of L-glutamic acid, L-lysine and DL-cysteine residues, the amino acid composition of which was approximately the same as that derived from the starting monomer mixture. *Anal.* Calcd. for $[(C_5H_7O_3N)_{20}(C_6H_{12}ON_2\cdot HI)_{20}(C_3H_5ONS)_2]_n$: I, 32.2; N, 10.9; amino-N, 3.54. Found: I, 32.1; N, 10.8; amino-N, 3.46. This polypeptide hydroiodide was soluble in water, methanol and ethanol, and gave positive biuret and nitroprusside reaction.

When the foil, made on the glass plate from its methanolic solution, was soaked in commercial (not purified) ether overnight, it became insoluble in water and colored yellowish brown, due to the liberation of iodine (this color vanished by soaking in very dilute alkali). This insoluble matter is considered to be a network polypeptide in which cysteine residues were converted into cystine ones.

(1) K. H. Meyer, *Biochem. Z.*, **214**, 253 (1929); *Experientia*, **7**, 361 (1951).

(2) W. Kuhn, B. Hargitay, A. Katchalski and H. Eisenberg, *Nature* **165**, 514 (1950).

(3) A. Katchalski and H. Eisenberg, *ibid.*, **166**, 267 (1950).

(4) W. Kuhn, *Experientia*, **5**, 318 (1949).

(5) A. Katchalski, *ibid.*, **5**, 319 (1949).

(6) J. W. Breitenbach and H. Karlinger, *Monatsh. Chem.*, **80**, 311 (1949).

A piece of this foil, which was swelled (11%) in distilled water, showed strong dilation in dilute acid or alkali and then contracted to its initial length in pure water. This change was isotropic and the linear dilation in 0.01 *N* HCl and 0.01 *N* NaOH was 35 and 45%, respectively.

A piece of metal, attached to the one end of a strip made from the foil, was carried up and down reversibly following the *p*H change of its surrounding medium (Fig. 1).

Its elongation, observed in water and 0.01 *N* HCl, was proportional to the weight of load (observed range of it was up to about 2,000 times the dry weight of the strip per 1 cm. long).

Further studies are required for a quantitative theoretical treatment of these phenomena and the comparison with muscular contraction, though it is clearly demonstrated that this synthetic amphoteric polypeptide network can contract at its isoelectric region and dilate on both the acidic and alkaline sides.

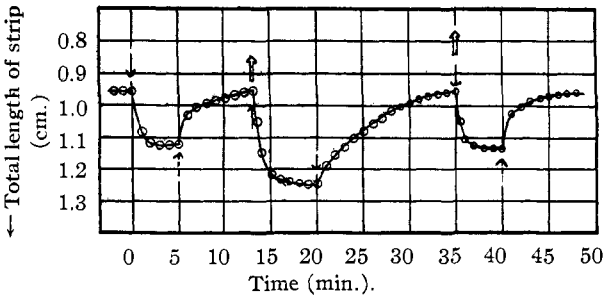

Fig. 1.—Reversible lifting and lowering of a load by a strip of amphoteric polypetide network: weight of dry strip (0.764 × 0.038 × *ca.* 0.003 cm.) 0.065 mg.; weight of load 5.07 mg.; medium 15 ml. 0.005*N* NaCl; ↓, acid (3 ml. 0.01*N* HCl) added; ↑, alkali (3 ml. 0.01*N* NaOH) added; ⇑, 6 ml. medium removed before addition of acid or alkali.

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BOOK REVIEWS

Rocks for Chemists—An Introduction to Petrology for Chemists and Students of Chemistry. By S. JAMES SHAND, Newberry Professor Emeritus of Geology in Columbia University, New York. Pitman Publishing Corporation, 2 West 45th Street, New York 36, N. Y. 1952. xii + 178 pp. 14.5 × 22 cm. Price $4.50.

Solution of the problems of the origin of rocks can come only as experimental work in physics and chemistry is combined with accurate geological field work. Interpretation of field data without the firm foundation of chemical principles properly understood and applied is valueless. One of the chief purposes of *Rocks for Chemists* is the creation of new interest on the part of chemists in the complex problems of the origin of rocks. Since the book is primarily for chemists, one might suppose that it would present important chemical aspects of the origin of all rocks. But this has not been done. More than three-quarters (105 pages) of the short book is devoted to eruptive rocks and their origin. Only 31 pages deal with metamorphic and sedimentary rocks.

A more appropriate title would have been *Eruptive Rocks for Physical Chemists*. Yet the book passes by much of the recent basic work on the physical chemistry of aqueous solutions of rock forming components. Hydrothermal solutions, derived from magmas, are considered in passing only, though these end products of differentiation effect profound changes on the parent and invaded rocks as well as giving rise to most concentrations of metallic ore minerals.

Elsewhere in the field of igneous rock petrology Dr. Shand has presented his own views to the exclusion of other widely held and strongly supported theories with which he does not agree. This is particularly true in his discussion of the origin of granite. Summary dismissal of the ideas of many geologists, who, on the basis of detailed field study, believe in the transformation of certain sedimentary rocks into granites by replacement through ionic diffusion, is hardly justified by the chemical data so far available. More study of ionic diffusion in silicate systems under conditions of high temperature and pressure is necessary.

Dr. Shand claims that sedimentary rocks do not offer as interesting problems as the eruptive rocks. This is the point of view of the igneous rock petrologist. A great number of geologists will disagree. In the pages on sedimentary rocks there is a superficial and even erroneous statement of the chemical aspect of sedimentary rock origin Such statements as "Most limestone begins as a simple accumulation of shells and shell fragments" and "Since no shells are so rich in magnesia as [$CaMg(CO_3)_2$], dolomite must be formed by exchange of bases between calcium carbonate and the magnesian salts held in solution by sea water" show a disregard for the complexities of carbonate rock origin, which is a field of research for intimate coöperation between chemists, biologists and geologists. With regard to the second statement quoted, some dolomites show clear evidence of having undergone base exchange in the presence of circulating ground water and, more locally, hydrothermal solutions. The use of the term *rock flour* with reference to shales is incorrect.

Chemists would be interested in the extremely complex problems in physical chemistry presented by the metamorphic rocks. In view of the carefully analytical studies recently published about these rocks and their origin, the 20 pages devoted to this topic are neither ample nor searching. Moreover, Dr. Shand, after showing that schists are complex equilibrium assemblages, and pointing out the unique place held by garnet because of the interchangeability of various bivalent and trivalent ions in the crystal lattice, says, in the last paragraph of the book, that "in the metamorphism of any rock which contains the components of garnet, that mineral will be formed in preference to others." In his concluding statement he suggests that, rather than indicating grades of intensities of metamorphism, assemblages of metamorphic minerals simply indicate an excess of certain components over the amount which may be incorporated in garnet. This speculation is not justified in view of much recent, careful field observation which clearly shows that metamorphic zones may be traced with great accuracy across lithologic boundaries.

Rocks for Chemists presents a partial statement of the status of petrology of igneous rocks in the light of selected chemical data. The book fails to present the equally important problems of sedimentary and metamorphic rocks. The narrowness of the views presented does injustice to the complicated variety of problems still unsolved and to many chemically minded geologists who, with the same facts and many others not presented, reach opposing conclusions.

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