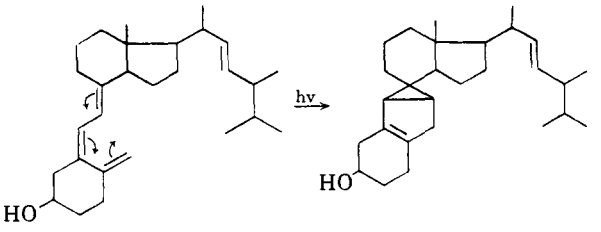
is both exocyclic to a six or larger membered ring originally containing the cyclopropane-ene system and conjugated to a ketone in a six or larger membered ring.

The most likely structure which could arise from vitamin D_2 and contain the structural requirements is shown below.



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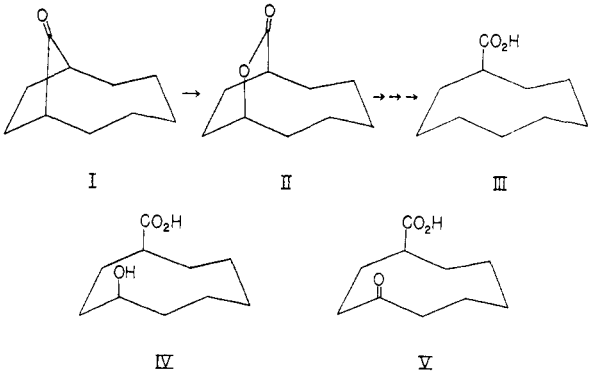
RECEIVED MAY 26, 1958

A NEW METHOD FOR THE SYNTHESIS OF BRIDGED RING KETONES AND MEDIUM SIZE RING COMPOUNDS

Sir:

Seventeen years ago a brief report from the Leverkusen laboratories appeared[1] in which the reaction between cyclohexanone and 1,4-bisdiazobutane was described as yielding a C_{10} product with a terpene-like odor. The structure of this material now has been established as 10-ketobicyclo[5,2,1]decane (I) by this series of reactions: Compound I, prepared in *ca.* 25% yield by the *in situ* ring enlargement procedure[2] from N,N'-dinitroso - N,N' - dicarbethoxy - 1,4 - diaminobutane[3] and cyclohexanone, m.p. 113–115° (clear at 120°), $\bar{\nu}_{max}^{liquid}$ 1735 cm.$^{-1}$ (C=O in 5-membered ring), (*anal.* found for $C_{10}H_{16}O$: C, 78.63; H, 10.37) was converted to the lactone II with peroxytrifluoroacetic acid,[4] m.p. 96–98° (*anal.* found for $C_{10}H_{16}O_2$: C, 70.89; H, 9.38; saponif. equiv. 167.9). The lactone (II) was heated with thionyl chloride in benzene solution,[5] treated with ethanol, and subjected to catalytic hydrogenation (one mole equivalent absorbed). The resulting product was saponified, converted to the acid chloride, and treated with aniline to yield the anilide of the known cyclononanecarboxylic acid,[6] m.p. 140–141° (*anal.* found for $C_{16}H_{23}NO$: C, 78.36; H, 9.39). Thus, the presence of a 5-membered ring (infrared) and a 9-membered ring taken in conjunction with a simple interpretation of the course of the reaction[2] leaves structure I as the most reasonable one. Further support for I is provided by the facile formation of a dibromide, m.p. 134–135° (*anal.* found for $C_{10}H_{14}Br_2O$: C, 39.05; H, 4.77) and by the base-catalyzed exchange of two hydrogen atoms for deuterium atoms. These latter reactions indicate the compound to be readily, a fact not unexpected from a consideration of the molecular model of I, although this structure resides at the edge of Bredt rule territory.[7] The ring enlargement of cycloalkanones with bis-



diazoalkanes provides a method for the synthesis of certain bicyclic systems (carbobicyclo[5,2,1] systems apparently have not been prepared previously) as well as a method for the synthesis of medium size carbocyclic ring compounds. The potentiality of the latter is suggested by the conversion of II to 4-hydroxycyclononanecarboxylic acid (IV), m.p. 86–87.5° (*anal.* found for $C_{10}H_{18}O_3$: C, 64.68; H, 9.58) and to 4-ketocyclononanecarboxylic acids (V), m.p. 33–35° (*anal.* found for $C_{10}H_{16}O_3$: C, 64.81; H, 8.55). Accompanying I are other materials, the structures of which have yet to be elucidated.

Acknowledgment.—This research was supported, in part, by grants-in-aid from the National Science Foundation and the Office of Ordnance Research.

(1) Petersen, U. S. Dept. of Commerce, Office of Technical Service Report PB 694 (1941).

(2) C. D. Gutsche, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 364.

(3) C. M. Samour and J. P. Mason, THIS JOURNAL, **76**, 441 (1954).

(4) W. D. Emmons and G. B. Lucas, *ibid.*, **77**, 2287 (1955).

(5) J. Cason, C. E. Adams, L. L. Bennett, Jr., and U. D. Register, *ibid.*, **66**, 1764 (1944).

(6) K. Schenker and V. Prelog, *Helv. Chim. Acta.*, **36**, 896 (1953). We are indebted to Professor Prelog for carrying out the melting point and infrared comparisons with our sample.

(7) F. S. Fawcett, *Chem. Rev.*, **47**, 219 (1950).

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RECEIVED JUNE 12, 1958

DEPENDENCE OF THE OPTICAL ROTATORY POWER OF PROTEINS ON DISULFIDE BONDS

Sir:

It has been known for a long time that most of the native proteins are levorotatory and that their rotation on denaturation increases considerably in the levo direction. An increase in levorotation also has been observed when the helical form of polyamino acids in non-polar solvents was converted into a random coil form by adding increasing amounts of a polar solvent.[1,2] It has been suggested,[3,4] therefore, that the decrease in levorotation

(1) P. Doty, J. H. Bradbury and A. M. Holtzer, THIS JOURNAL, **78**, 947 (1956); P. Doty, A. M. Holtzer, J. H. Bradbury and E. R. Blout, *ibid.*, **76**, 4493 (1954).

(2) E. R. Blout and M. Idelson, *ibid.*, **78**, 497 (1956).

(3) J. T. Yang and P. Doty, *ibid.*, **79**, 761 (1957).

(4) G. Markus and F. Karush, *ibid.*, **79**, 134 (1957).

of proteins after cleavage of their dithio bonds also might be caused by transformation of a random coil form of their peptide chains into an α-helix. Since L-cystine differs from all the other natural α-amino acids by its extremely high levorotation, we investigated the optical rotation of some typical proteins in the native state and after oxidation of the dithio bonds.

Crystalline bovine serum albumin was obtained from Armour Laboratories, edestin from the Nutritional Biochemicals Corporation. Ovalbumin was prepared from hens' eggs.[5] The protein samples were oxidized by performic acid.[6] The excess of performic acid was reduced by ethanol and the oxidized protein precipitated with 5 M sodium chloride solution. The protein suspension was dialyzed and lyophilized. The optical rotation of both the native and the oxidized proteins was measured after redissolving them in 88% formic acid. The results are presented in Table I.

TABLE I

	Bovine serum albumin	Ovalbumin	Edestin
$[\alpha]^{25}D$ native	-81.7 ± 0.8	-53.7 ± 0.5	-66.9 ± 0.6
$[\alpha]^{25}D$ oxidized	-59.2 ± 0.9	-48.8 ± 0.9	-60.5 ± 0.2
Mol. wt.[7]	69,000	46,000	50,000
Cystine residues per molecule	17	1	2
Change in rotation after oxidation ($\Delta[\alpha]D$			
Obsd.	$+22.5 \pm 1.2$	$+4.9 \pm 1.0$	$+6.4 \pm 0.6$
Calcd.	17.3	1.5	2.8

(5) R. A. Kekwick and R. K. Cannan, *Biochem. J.*, **30**, 227 (1936).

(6) M. E. Reichmann and J. R. Colvin, *Can. J. Chem.*, **33**, 163 (1955).

(7) G. R. Tristram in Neurath-Bailey (eds.), "The Proteins," Vol. I, p. 181 (1953).

The specific rotation of L-cystine in 88% formic acid was found to be $-285.0°$, that of L-cysteic acid $+5.5°$. Since one mole (240 g.) of cystine gives 2 moles of cysteic acid (338 g.), the increase in dextrorotation for a 1% solution of cystine is $(285.0/100) + (5.5 \times 338)/(100 \times 240) = +2.928$. If n is the number of cystine residues per protein molecule and M the molecular weight of the protein, the calculated increase in dextrorotation is $(240 \times 100 \times 2.928 \times n)/M = 70{,}272n/M$. It can be seen from Table I that the change in rotation increases with the cystine content of the proteins and that the calculated value of $\Delta[\alpha]D$ is of the same order as the observed value. A similar result was obtained with lysozyme where $\Delta[\alpha]D$ was $+15.6°$, and the calculated value $+19.1°$. We conclude that the large change in $[\alpha]D$ following performic acid oxidation of the dithio bridges in those proteins which are rich in dithio bonds is caused chiefly by destruction of the strained, hydrogen-bonded, structure of the cystinyl residues which has been described by Fieser,[8,9] and that other conformational changes of the peptide chains cause only minor changes in $[\alpha]D$.

Acknowledgments.—Support of this work by grants of the U. S. Public Health Service (#1852) and the National Science Foundation (#G 1296) to F. H. and by contracts of Indiana University with the U. S. Atomic Energy Commission (At-11-1-209) and the Office of Naval Research (NR 120-035) is gratefully acknowledged.

(8) L. F. Fieser, *Rec. trav. chim.*, **69**, 410 (1950).

(9) We are grateful to Drs. E. Campaigne and M. Carmack for discussion of these problems.

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RECEIVED MAY 15, 1958

BOOK REVIEWS

The Pentaerythritols. ACS Monograph No. 136. By EVELYN BERLOW, ROBERT H. BARTH and JOHN E. SNOW, Research Department, Heyden Newport Chemical Corporation, Garfield, New Jersey. Reinhold Publishing Corporation, 430 Park Avenue, New York 22, N. Y. 1958. vii + 317 pp. 16 × 23.5 cm. Price, $10.00.

The publication of this excellent, short monograph upon the pentaerythritols is an indication of the interest which has developed in the manufacture and uses of the pentaerythritols.

The pentaerythritols have been manufactured, commercially, for over twenty years, and have reached an annual U. S. peacetime production of close to 60,000,000 pounds. Practically all of the production is being used in the coatings industry.

The pentaerythritol industry has reached the stage where a monograph, such as this, serves a very useful purpose in that it provides a ready reference work for the executive, marketing, engineering, operating, research and patent personnel.

The work is divided into seventeen chapters, an author index and a subject index.

Chapter 1 is the Introduction. It is short, but gives an easy-to-read account of the discovery of pentaerythritol, its manufacturing growth and the manufacturers in the United States responsible for this growth.

Chapter 2 on the Preparation brings together about 194 references having a bearing upon the processes available for the manufacture of the pentaerythritols. It does not attempt to evaluate the substance of these references from standpoints of utility or theoretical soundness. It is, however, a very useful and thought-provoking chapter.

Chapter 3, which deals with the Physical Properties of the pentaerythritols, contains appreciable new material, particularly data relating to the solubility of pentaerythritols in a long list of solvents, and data relating to the infrared spectrum of pentaerythritol, of dipentaerythritol and of tripentaerythritol.

Chapter 4, dealing with the Physiological Properties is very short and lists only eight references. However, since it appears that the pentaerythritols are non-toxic, this chapter serves as an assurance of the safety involved in working with these products.

Chapter 5 pertains to Methods of Analysis. The methods described are very practical. However, no critical analysis