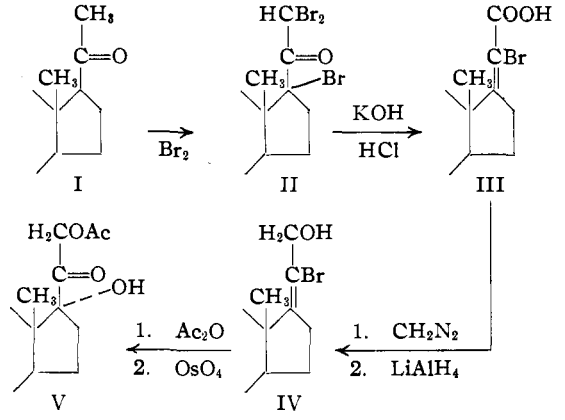
A NEW ROUTE TO THE CORTICAL SIDE CHAIN

Sir:

The conversion of the readily available bromopregnanolones to compounds of the cortical series having a dihydroxyacetone side chain has been achieved. The key steps involve a rearrangement of a tribromoketone and subsequent reduction of the product.



Bromination of pregnan-3(β)-ol-20-one acetate (I) with three moles of bromine yields the 17,21, 21-tribromo derivative (II), m. p. 196° (dec.), $[\alpha]^{25}D$ −3.4° (chloroform). Calcd. for $C_{23}H_{33}O_3Br_3$: Br, 40.1. Found: Br, 40.3. Rearrangement with alcoholic potash yields 17-pregnen-3(β)-ol-20-bromo-21-oic acid (III), m. p. 273° (dec.), $[\alpha]^{25}D$ + 41° (dioxane). Calcd. for $C_{21}H_{31}O_3Br$: C, 61.4; H, 7.6; Br, 19.4. Found: C, 62.0; H, 7.7; Br, 19.1. Reduction of the bromo acid with hydrogen and platinum catalyst gives pregnan-3(β)-ol-21-oic acid, m. p. and mixed m. p., 220°.[1] Lithium aluminum hydride reduction of the methyl ester of III yields the unsaturated 20-bromo-21-ol (IV), m. p. 253° (dec), $[\alpha]^{25}D$ +53° (dioxane). Calcd. for $C_{21}H_{33}O_2Br$: C, 63.5; H, 8.4. Found: C, 63.4; H, 8.5. Treatment of the diacetate of IV with osmium tetroxide in ether yields pregnan-3(β),17(α),21-triol-20-one diacetate (V), m. p. 153°, $[\alpha]^{28}D$ +49° (dioxane). Calcd. for $C_{25}H_{38}O_6$: C, 69.1; H, 8.8. Found: C, 68.8; H, 8.8. Hydrogenation of V gives the same tetrol obtained by the lithium aluminum hydride reduction of methyl 17-pregnen-3(β)-ol-21-oate with subsequent hydroxylation (OsO_4), isolated as the triacetate, m. p. and mixed m. p. 184°, $[\alpha]^{28}D$ +55° (chloroform). Calcd. for $C_{27}H_{42}O_7$: C, 67.8; H, 8.9. Found: C, 67.4; H, 8.9.

We thank Parke, Davis and Company for their help.

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RECEIVED NOVEMBER 19, 1949

(1) Marker, Crooks and Wagner, THIS JOURNAL, **64**, 817 (1942).

HOMOLOGATION OF ALCOHOLS

Sir:

The conversion of an alcohol to the primary alcohol containing one carbon atom more than the original is usually a tedious procedure. We wish to report a simple one-step homologation reaction. The process consists in treating the alcohol with synthesis gas (carbon monoxide and hydrogen) in the presence of a cobalt catalyst under conditions resembling those employed in the oxo reaction.

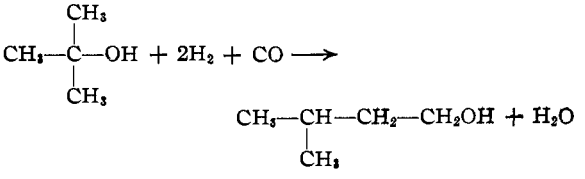
The oxo or hydroformylation reaction consists of the conversion, by means of synthesis gas, of an olefin to a mixture of aldehydes containing one carbon atom more than the starting material.

$$R{-}CH{=}CH_2 + CO + H_2 \xrightarrow{Co} R{-}CH_2{-}CH_2{-}CHO + R{-}CH(CH_3)CHO$$

As developed in Germany, a mixture of olefins secured from the Fischer–Tropsch reaction was usually used as the starting material. The aldehydes resulting from the oxo reaction were then converted in a separate step, to a mixture of alcohols which were of value for detergent manufacture. It has been reported recently[1] that olefins may be converted in one step directly to the alcohol if the usual oxo reaction is operated at slightly higher temperatures. That our homologation reaction need not proceed *via* an olefin intermediate followed by a one-step hydroformylation–hydrogenation is shown by the fact that benzyl alcohol is converted to β-phenylethyl alcohol under our conditions: $PhCH_2OH + 2H_2 + CO \rightarrow PhCH_2CH_2OH$. Other conversions we wish to report consist of the formation of *n*-butyl alcohol and of isobutyl alcohol from isopropyl alcohol and of isoamyl alcohol from *t*-butyl alcohol. *n*-Propyl alcohol gave a mixture of *n*-butyl and isobutyl alcohols but the reaction proceeded so slowly at 180° that part of the initial products was transformed by further homologation to higher alcohols.

We are inclined to believe that the homologation reaction is an acid ($HCoCO_4$) catalyzed reaction that proceeds *via* a carbonium ion according to a mechanism that will be discussed in detail later.

In a typical experiment, *t*-butyl alcohol (86 g., 1.3 moles) and cobaltous acetate (7.0 g., 0.03 mole) were placed in an 0.5-liter stainless steel autoclave and heated with synthesis gas (3200 p. s. i., $1H_2$:1CO) at 160–180° for one and one-half hours Gas absorption was 89% of the theoretical according to the equation



There was obtained a 63% yield of isoamyl alco-

(1) Wender, Levine and Orchin, Abstracts of the Atlantic City meeting of the American Chemical Society, September 19–23, 1949

hol; α-naphthylurethan, m. p. 65.6–66.3°; mono ester with 3-nitrophthalic anhydride, m. p. 165.3–166.4°. Somewhat better results were obtained with cobaltous oxide as catalyst.

Benzyl alcohol gave toluene (49%) and β-phenylethyl alcohol (26%); α-naphthylurethan, m. p. 117.5–118.5°. Distillation of the alcohol from molten potassium hydroxide gave an 86% yield of styrene, identified through its dibromide.

Isopropyl alcohol gave 11% of a mixture of *n*-butyl and isobutyl alcohol; the former was identified by its infrared spectrum and the latter by its phenylurethan, m. p. 84.6–85.5°. *n*-Propyl alcohol reacted slowly at 180° to give a mixture of butyl, isobutyl, isoamyl and *n*-amyl alcohols, identified by their infrared absorption spectra.

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RECEIVED OCTOBER 10, 1949

NEW BOOKS

Radioactive Indicators. Their Application in Biochemistry, Animal Physiology, and Pathology. By GEORGE HEVESY, Institute for Research in Organic Chemistry, University of Stockholm, Sweden; Institute for Theoretical Physics, University of Copenhagen, Denmark. Interscience Publishers, Inc., 215 Fourth Avenue, New York 3, N. Y., 1948. xvi + 556 pp. Illustrated. 16 × 24 cm. Price, $10.00.

Thirty-six years ago the first paper on the use of radioactive indicators was published by Paneth and Hevesy. They first determined the solubility of some lead compounds and for several years were the only research workers applying this new tool. Ten years later, in 1923, Hevesy reported the first biological application of radioactive indicators: a study of the absorption and translocation of lead in plants. The present book is the most recent of a long series of publications by this pioneer in applied radiochemistry.

Chemists not primarily concerned with life science research will find little of direct interest in this book since it is a reference book written as a very extensive review article of the applications of radioactive indicators in biochemistry, animal physiology and pathology.

The first three chapters cover the production, availability and measurement of radioactive tracers. These chapters and the next two on atomic interchange and applications in chemical analysis do not fall within the province of the author's major interests and suffer as a consequence thereof. They represent an uncritical compilation of some of the literature and include such items as a copy of the 1947 catalog and price list of radioisotopes available from the U. S. A. E. C. Three long tables showing the decay of Na^{24}, K^{42} and P^{32} also seem unnecessary in a book of this type. The remaining eighty per cent. of the book is a substantial contribution to the literature of radioactive indicators, representing as it does a review of thirteen years of intensive work by many investigators in a very active field of research.

This section follows a logical pattern, starting with the general considerations of absorption, distribution and excretion of more than twenty-five elements, as simple inorganic species, in the whole animal organism. This is followed by a discussion of the problems associated with the transport of ions and compounds across the many types of membranes in living systems. Metabolic studies, including intermediary metabolism, are treated next. This section closes with a survey of the new information obtained from radioactive indicator studies of the special organs; the skeleton and red cells. The shortcomings of radioactive indicators in biology treated in the final chapter provide a timely warning for overenthusiastic readers.

Throughout the book many of the data from the original articles are reproduced in tables and graphs and detailed references are given. A Segre chart is included in an attached envelope in the back of the book. The author index and subject index are both excellent as they should be for this type of reference book.

Since the use of radioactive indicators in the fields of biochemistry, animal physiology and pathology is increasing so rapidly, Hevesy's "Radioactive Indicators" may be the last complete review of these fields. It will serve well as a point of departure for subsequent reviews of the accumulating knowledge, during the next few years.

JOHN W. IRVINE, JR.

Chemistry of Specific, Selective and Sensitive Reactions. By FRITZ FEIGL, Eng., Dr. Sc., Laboratory of Mineral Products, Ministry of Agriculture, Rio de Janeiro, Brazil; formerly Professor of Analytical and Inorganic Chemistry at the University of Vienna. Translated by Ralph E. Oesper, Professor of Chemistry, University of Cincinnati, Ohio. Academic Press, Inc., New York, N. Y., 1949. xiv + 740 pp. 15 × 23 cm. Price $13.50.

Perhaps few books have been written under greater hardships and handicaps than this one. The author began the laborious task of collecting and preparing material long before World War II but this was all lost during his flight from Europe and he had to make a new start after getting relocated in Brazil. The manuscript was written in German and translated into English by Professor R. E. Oesper, to whom the author pays especial thanks for his technical advice, patience ("even with last minute changes"), and deep understanding of the aims of the work. The "earmarks" of a translation, so often evident in English translations of technical books, are pleasingly missing and the reviewer found no serious typographical errors while reading the book from cover to cover.

The contents of the book and the method of presentation were chosen with three groups of readers in mind: (1) "those who wish to know the chemical basis of many modern analytical procedures," (2) "those who are actively engaged in research in analytical chemistry or in related fields," and (3) "those interested in experimental chemistry as a part of science which is still a fertile field for the trained and alert investigator." This was indeed an ambitious undertaking and no one is better qualified for such a task than Fritz Feigl who for more than a quarter of a century has made outstanding contributions to the