TABLE I

Additions	TPNH oxidized (mμmoles)	C^{14}-substrate incorporated into palmitate (mμmoles)
None	18.0	. .
1-C^{14}-acetyl CoA (12 mμmoles)	32.2	1.80
same +		
acetaldehyde (1000 mμmoles)	32.2	1.90
1-C^{14}-acetate (320 mμmoles)	18.0	0.00
2-C^{14}-malonate (1000 mμmoles)	18.2	0.00
1-C^{14}-butyryl CoA (30 mμmoles)	18.2	1.10
1-C^{14}-octanoyl CoA (50 mμmoles)	20.0	3.00

Each cuvette contained 20 μmoles of potassium phosphate buffer *p*H 6.5, 50 mμmoles of TPNH, 50 mμmoles of synthetic unlabeled monomalonyl CoA, other substrates as indicated, 200 μg. of R_{2gc} and H_2O to 0.4 ml. Incubated for 10 min. at 38°.

R_{2gc}, as prepared, does contain an enzyme which decarboxylates malonyl CoA to CO_2 and acetyl CoA (as measured by the enzymatic formation of citrate). This would explain why malonyl CoA in the absence of added acetyl CoA can form palmitate in the presence of R_{2gc} and TPNH (Table I). R_{2gc} does not contain enoyl hydrase, β-hydroxyacyl dehydrogenase or thiolase nor does it catalyze the oxidation of TPNH by acetyl CoA, acetoacetyl CoA, β-hydroxybutyryl CoA, crotonyl CoA, butyryl CoA, Δ^{2-3}-hexenoyl CoA and octanoyl CoA. The oxidation of TPNH in this system requires the combined presence of malonyl CoA and some unsubstituted fatty acyl CoA (C_2, C_4, C_6 etc.). None of the substituted intermediates of the β-oxidation sequence can replace these fatty acyl CoA esters. These observations suggest a possible mechanism of fatty acid synthesis

$$\mathrm{CH_3COCoA + CO_2 + ATP \xrightarrow[R_{1gc}]{\text{Biotin-containing}} HOOCCH_2COCoA}$$

$$\mathrm{CH_3COCoA + HOOCCH_2COCoA \xrightarrow{R_{2gc}}}$$

$$\Big[\mathrm{CH_3COCH(COOH)COCoA \xrightarrow{TPNH} CH_3CHOHCH(COOH)COCoA \xrightarrow{-H_2O} CH_3CH{=}C(COOH)COCoA \xrightarrow{TPNH} CH_3CH_2CH(COOH)COCoA \longrightarrow}\Big]$$

$$\mathrm{CH_3CH_2CH_2COCoA + CO_2}$$

The butyryl CoA formed can condense with another molecule of malonyl CoA with the formation of the β-ketodicarboxylic acid as indicated above.

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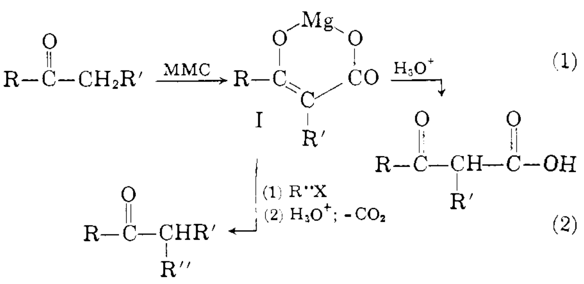
CHELATION AS A DRIVING FORCE IN SYNTHESIS. II. USE OF MAGNESIUM METHYL CARBONATE IN THE CARBOXYLATION AND ALKYLATION OF KETONES

Sir:

A previous communication[1] described the use of magnesium methyl carbonate (MMC) for the carboxylation of nitroparaffins. Further investigation has revealed that this reagent readily converts ketones to β-keto acids (eq. 1). Equally important from a practical standpoint is our finding



that the intermediate magnesium salts of β-keto acids (I) may be alkylated *in situ*. Thus the path indicated by eq. 2 is experimentally a simple method for the alkylation of ketones.

Treatment of acetophenone with 3–4 molar equivalents of MMC in dimethylformamide at 110–120° for one hour, and then acid hydrolysis, furnished a 68% yield of benzoylacetic acid, m.p. 99–100° dec. (reported,[2] 100° dec.). 1-Indanone was converted in 91% yield by the same technique to 1-indanone-2-carboxylic acid, m.p. 100–101° dec. (reported,[3] 98–100° dec.).

Cyclohexanone (1.82 g., 0.0186 mole) was heated with 80 ml. of 1.94 *M* MMC solution at 120–130° for 6 hours. After hydrolysis the crude product was extracted into ether, dried, and treated with ethereal diazomethane. Crystallization from methanol gave 1.90 g. (48%) of dimethyl cyclohexanone-2,6-dicarboxylate, m.p. 139–140° (reported[4] m.p. 142–143°) identical with an authentic specimen.[5] Alternatively the free diacid, m.p. 123° dec., neut. equiv., 99.5 (reported[6] m.p. 120–140° dec.) could be isolated by crystallization from ether–petroleum ether. Evidence for the importance of the coördinating properties of magnesium in these reactions may be seen by comparing this result with that obtained[7] by treatment of cyclohexanone with sodium ethyl carbonate.

1-Tetralone was treated with MMC solution at 120–130° for one hour, and to the cooled mixture an excess of benzyl bromide was added. Heating on the steam-bath for 6 hours, acid hydrolysis, and decarboxylation provided a 72% yield of 2-benzyl-1-tetralone, b.p. 150–155°(0.4 mm.), m.p. 51–53° (reported,[8] b.p. 176°(1 mm.), m.p. 53–54°).

When acetophenone was heated with MMC (4 equiv.) as described above, followed by methyl iodide (3 equiv.), a 74% yield of isobutyrophenone was obtained after decarboxylation. Propiophenone was not isolated, even when less than two equivalents of alkylating agent was used. Evidently the chelate salt from 2-benzoylpropionic acid (I, R = C_6H_5, R′ = CH_3), which would be formed rapidly from the initial alkylation product

(1) M. Stiles and H. L. Finkbeiner, THIS JOURNAL, **81**, 505 (1959).

(2) E. Beckmann and T. Paul, *Ann.*, **266, 1** (1891).

(3) R. H. Wiley and P. H. Hobson, THIS JOURNAL, **71,** 2429 (1949).

(4) F. F. Blicke and F. J. McCarty, *J. Org. Chem.*, in press.

(5) Sample provided through the courtesy of Drs. R. E. Ireland and P. W. Schiess.

(6) J. W. Cook, J. D. Loudon, and D. K. V. Steel, *J. Chem. Soc.*, 530 (1954).

(7) J. I. Jones, *Chem. and Ind.* (*London*), 228 (1958).

(8) W. Borsche, P. Hofmann and H. Kühn, *Ann.*, **554**, 23 (1943).

by the action of excess MMC, is alkylated as rapidly as the salt of benzoylacetic acid.

The carboxylation and alkylation technique described here is remarkably free of side reactions, such as self-condensation of the ketones. This, together with the availability and stability of MMC solutions, suggests that the method will find considerable application in synthesis.

The author is grateful to Mr. Herman L. Finkbeiner for interesting discussions and for gifts of MMC.

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RECEIVED APRIL 15, 1959

BOOK REVIEWS

The Metabolism of Sulfur Compounds. By LESLIE YOUNG, D.Sc., Ph.D., F.R.I.C., Professor of Biochemistry in the University of London, St. Thomas's Hospital Medical School, London, and GEORGE A. MAW, Ph.D., F.R.I.C., Senior Lecturer in Biochemistry, St. Thomas's Hospital Medical School, London. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y. 1958. 180 pp. 12.5 × 19 cm. Price, $3.00.

The authors of this pocket-size monograph have done an admirable job of presenting a concise account of the metabolism of sulfur compounds in animals and bacteria. It is a general account which touches on thiols, disulfides, thiol ethers, sulfonium compounds, sulfoxides, sulfones, sulfonic acids, sulfuric acid esters, and a further miscellaneous assortment of sulfur compounds. In the opinion of the reviewer, this monograph makes its appearance at a time when it is needed. Within recent years, there has been an awakening of interest in the metabolism of sulfur compounds. In part this has been due to the availability of S^{35} and in part to the fortuitous discovery of compounds like biotin, lipoic acid, Coenzyme A, and "active sulfate" because of improved separation processes. An unusually large number of papers and an occasional detailed review on a limited phase of the chemistry and metabolism of sulfur-containing compounds have appeared. These more recent advances have been critically interwoven with observations of the past into a pleasantly readable account. The monograph should, therefore, prove useful as a source for an over-all up-to-date (1958) view for the beginning student and the more advanced worker in the field. In addition, the monograph may well serve as a source of key references on phases of sulfur metabolism of particular interest to the reader; some eight hundred references are cited.

The monograph is recommended wholeheartedly to anyone with a general interest in biochemistry as well as to those with a particular interest in the metabolism of sulfur compounds.

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Elementary Statistical Physics. By C. KITTEL, Professor of Physics, University of California, Berkeley, California. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y. 1958. ix + 228 pp. 15.5 × 23.5 cm. Price, $8.00.

Books on statistical mechanics are less numerous than those covering other topics of comparable importance in physics. Possibly not more than half a dozen have appeared in the English language in the last decade, and probably one could not name two that cover the same range of topics at the same level. If only for this reason, any new book on the subject is a welcome addition to the physicist's library.

Professor Kittel's book covers in compact form a considerable range of topics, including some that are not usually treated even in more extensive and advanced treatises. The problem is approached from the classical viewpoint by the Gibbs method of ensembles, which not only is the most satisfactory from the logical standpoint, but also best lends itself to the extension to systems of interacting particles. The microcanonical, canonical and grand-canonical ensembles are introduced in this order and thermodynamic quantities are defined. The standard applications to ideal gases are developed. Quantum effects are considered, including the behavior of Bose–Einstein and Fermi-Dirac gases at low temperatures and high densities, and the theory of the thermal radiation is included. Welcome additions in comparison with most standard textbooks are a brief but clear treatment of the density matrix method, and a discussion of "negative temperatures," a somewhat mystifying term by which it has become customary to describe states of spin systems when the upper levels are more densely populated than the lower levels.

The next part of the book deals with miscellaneous topics, such as fluctuations, noise, correlations, and the Onsager relations in the thermodynamics of irreversible processes. The third and last part discusses transport phenomena. Such properties as electrical and thermal conductivities, viscosity, etc., are derived from the Boltzmann equation. An appendix gives a more detailed treatment of some of the mathematics used in statistical mechanics.

Professor Kittel has successfully accomplished his purpose of giving a modern, compact survey of statistical mechanics at the beginning graduate level. He has stressed the basic principles and chosen, among the limited number of applications that could be included in a book of this size, those best suited to illustrate the principles themselves. With one exception, no attempt was made to discuss systems of interacting particles, such as imperfect gases or the Ising model of a ferromagnet. This may have been a wise decision, as it is known that even when simplified to the point of losing most of their physical significance, such problems still present formidable mathematical difficulties and can only be attacked by cumbersome approximation methods.

The book is well written, apparently almost free of errors or misprints, and presented in pleasant typographical form. A useful feature is the bibliography at the beginning of each section.

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Theoretical Principles of Organic Chemistry. Volume II. By WALTER HÜCKEL, Dr. Phil., Professor of Pharmaceutical Chemistry, Tübingen University (Germany); Formerly Professor of Organic Chemistry at the University and Technische Hochschule of Breslau. Translated from the corrected 7th German Edition by F. H. RATHMANN, Associate Professor of Organic Chemistry, North Dakota Agricultural College, Fargo, N. D. (U.S.A.). D. Van Nostrand Company, Inc., 120 Alexander Street, Princeton, N. J. 1958. xi + 1046 pp. 17.5 × 25.5 cm. Price, $19.00.

The range of subjects discussed in this second volume of Hückel's "Theoretical Principles of Organic Chemistry" is indicated by the titles of the ten chapters: Chapter XI. Theoretical Consideration of Physical Properties. Thermal Magnitudes; Chapter XII. The Electrical Properties of Molecules; Chapter XIII. Behavior of Matter (Sub-