cis-3-hexene, there was obtained a 35.5% yield of pure *cis*-1,2-diethylcyclopropane (b.p. 93.5°, $n^{25}D$ 1.4035; *anal.* Calcd. for C_7H_{14}: C, 85.63; H, 14.37. Found: C, 85.89; H, 14.32). An analogous experiment with pure *trans*-3-hexene gave a 15.5% yield of pure *trans*-1,2-diethylcyclopropane (b.p. 86.5°, $n^{25}D$ 1.3982; *anal.* Found: C, 85.54; H, 14.49). In both reactions, vapor-phase chromatographic and infrared spectral analysis of the reaction mixtures showed only the presence of the starting olefin and the corresponding cyclopropane. Similar data from known mixtures of the olefins and cyclopropanes indicated that the analytical methods were capable of defining purity to at least 0.5%.

These results clearly establish the stereospecificity and discrimination in the reaction of an olefin with methylene iodide and zinc–copper couple. After this work was completed, a report[7] appeared stating that "methylene iodide and finely divided zinc–copper couple react with *cis*- and *trans*-butene to give *cis*-1,2-dimethylcyclopropane, *cis*-pentene and 2-methyl-2-butene, and *trans*-1,2-dimethylcyclopropane, *trans*-pentene and 2-methyl-2-butene, respectively. These reactions are comparable to that of diazomethane with *cis*- and *trans*-butene.[4]" Since experimental details were lacking in this brief account, we are unable to offer any explanation for these results, which apparently conflict with our own.

Studies of the methylene iodide/zinc–copper couple system, including the preparation of isotopically labeled cyclopropanes (from CD_2I_2 and $C^{14}H_2I_2$), are continuing.

(7) W. von E. Doering and P. M. LaFlamme, *Tetrahedron*, **2**, 75 (1958). Reference 4 in the quotation refers to W. von E. Doering and P. M. LaFlamme, THIS JOURNAL, **78**, 5447 (1956).

CONTRIBUTION NO. 502 FROM THE
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CALCIUM DIMETHYL, STRONTIUM DIMETHYL, AND BARIUM DIMETHYL

Sir:

We report the preparation and some properties of three new compounds, calcium dimethyl, $Ca(CH_3)_2$, strontium dimethyl, $Sr(CH_3)_2$, and barium dimethyl, $Ba(CH_3)_2$. Evidence of organo-compounds of these metals in solution had been known at least since 1905[1-4] but no such compound had been isolated and characterized, except for some complexes with organo-zinc compounds,[5-9] until the present work.

Calcium, strontium and barium, when rasped from bulk metal to a granular form, in an atmosphere of helium, react readily with methyl iodide in anhydrous pyridine. The solutions quickly become highly colored, and insoluble solids precipitate. These apparently are pyridine complexes containing both methyl and iodine attached to metal, of composition dependent on the conditions. Refluxing, followed by prolonged extraction of these solids with fresh pyridine, reduces the iodine content leaving ultimately the dimethyl metal compound as an insoluble residue. Pyridine separates readily from all three dimethyl compounds when the solids are evacuated at room temperature.

The dry solids were analyzed by hydrolysis of 10–100 mg. samples and then measurement of evolved methane and standard gravimetric determinations of both metal and iodine. Calcd. for $Ca(CH_3)_2$: Ca, 57.2; CH_3, 42.8. Found: Ca, 58.5, 57.8; CH_3, 42, 40; I, 1.9, 1.4, 1.7. Calcd. for $Sr(CH_3)_2$: Sr, 74.5; CH_3, 25.5. Found: Sr, 72.7, 74.2, 73.3; CH_3, 23, 22; I, 3.5, 3.2. Calcd. for $Ba(CH_3)_2$: Ba, 82.0; CH_3, 18.0. Found: Ba, 81.6, 78.8, 79.1; CH_3, 17, 18; I, 2.6, 2.5. Assuming the residual iodine, which seems impossible to remove even by very prolonged extraction, to be present as the metal iodide, the dimethyl compounds appear to be of better than 95% purity.

These compounds are all pale in color and might well be white but for the residual iodide. They undergo no visible change in vacuum below 400°, above which darkening occurs. All three hydrolyze very rapidly, and promptly become incandescent when exposed to oxygen or carbon dioxide.

(1) E. Beckmann, *Ber.*, **38**, 904 (1905).
(2) H. Gilman and W. Schulze, THIS JOURNAL, **48**, 2463 (1926).
(3) Z. C. Glacet, *Bull. soc. chim. France*, **5**, 895 (1938).
(4) E. Kraus and A. v. Grosse, "Die chemie der metall-organischen Verbindungen," Borntraeger, Berlin, 1936, p. 123.
(5) F. Hein, E. Petzchner, K. Wagler and F. Segitz, *Z. anorg. allgem. Chem.*, **141**, 161 (1924).
(6) H. Gilman, R. Meals, G. O'Donnell, and L. Woods, THIS JOURNAL, **65**, 268 (1943).
(7) H. Gilman and L. Woods, *ibid.*, **67**, 520 (1945).
(8) H. Gilman, A. Haubein and L. Woods, *ibid.*, **67**, 922 (1945).
(9) H. Gilman and J. C. Bailie, *ibid.*, **65**, 267 (1943).

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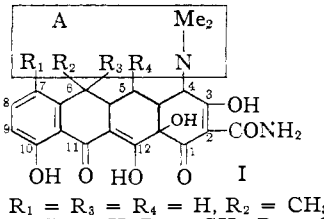
HYDROGENOLYSIS STUDIES IN THE TETRACYCLINE SERIES—6-DEOXYTETRACYCLINES

Sir:

Hydrogenolysis of tetracycline[1] under acidic conditions with palladium results in a mixture of products from which we have separated a new antimicrobial substance, *6-deoxytetracycline*, (Ia, m.p. of the hydrochloride, 245–246°, dec. *Anal.* Calcd. for $C_{22}H_{25}N_2O_7Cl$: C, 56.95; H, 5.38; N, 6.05. Found: C, 56.64; H, 5.50; N, 6.02). An analogous *6-deoxy compound* (Ib, m.p. of hydrochloride 250–251°, dec., *pK'*s 3.4, 7.7, ~9.7 (H_2O).



I

Ia, $R_1 = R_3 = R_4 = H$, $R_2 = CH_3$
Ib, $R_1 = R_3 = H$, $R_2 = CH_3$, $R_4 = OH$

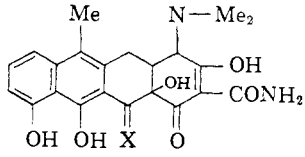
Anal. Calcd. for $C_{22}H_{25}N_2O_8Cl$: C, 54.93; H, 5.24; N, 5.82. Found: C, 54.86; H, 5.35; N, 5.75).

(1) Tetracyn is the registered trade-mark of Chas. Pfizer & Co., Inc., for the antibiotic tetracycline.

is obtained from oxytetracycline[2] under similar conditions. Structural assignments rest on composition, mode of formation, absorption spectra, dissociation constants and on the striking observation that the 6-deoxy compounds (lacking the C.6 benzyl hydroxyl group) *do not undergo* the very characteristic acid degradation to anhydrotetracycline (IIa) analogs observed with all previously known members of the tetracycline series.[3,4,6,8]

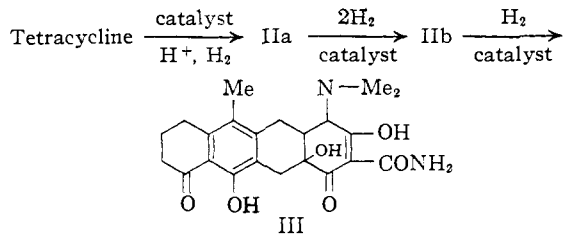
6-Deoxy compound formation also is observed with 6-demethyltetracycline[4] and with desdimethylaminotetracycline analogs.[5]

An acid catalyst apparently is required for 6-deoxygenation. However, in many instances the hydrogenolysis of tetracycline compounds is complicated by a novel effect of noble metal catalysts and hydrogen in promoting acid dehydration at the C.6-C.5a position to form anhydrotetracycline (IIa) analogs, which then, themselves, undergo



IIa, X = O
IIb, X = H_2

hydrogenation. Thus, in the case of tetracycline, an important companion reaction to 6-deoxy compound formation apparently proceeds as shown. Under appropriate conditions compound III (m.p. of the hydrochloride 239–240°, dec., λ_{max} 265 mμ, log ε 4.55, λ_{max} 346 mμ, log ε 3.72 (0.01 *N* HCl in methanol); *pK*'s 4.1, 8.4, ~12.2 (H_2O). *Anal.*



III

Calcd. for $C_{22}H_{27}N_2O_6Cl$: C, 58.60; H, 6.04; N, 6.22; Cl, 7.89. Found: C, 58.59; H, 6.03; N, 5.77; Cl, 7.97) may be obtained in good yield from either tetracycline or anhydrotetracycline. The structural assignment rests on its composition, mode of formation, acidity constants, ultraviolet chromophore (that of a substituted 8-hydroxy-1-tetralone[6]), and on the observation that the hydroxytetralone chromophoric group is unchanged by boiling alkali.

The *in vitro* antimicrobial spectra of 6-deoxytetracycline and 6-deoxyoxytetracycline are comparable to those of the parent substances though some differences are observed.[7] This observation is of particular significance to structure-activity studies since the 6-deoxy compounds complete a series[3,4,5,6,8] of variously substituted tetracyclines—obtained by both chemical and biochemical means—in which every substituent along the "upper periphery" of the basic structure (*cf.* segment A of structure I) has been altered without drastically changing *in vitro* antibacterial activity.

(2) Terramycin is the registered trade-mark of Chas. Pfizer & Co., Inc., for the antibiotic oxytetracycline.

(3) *Cf.* C. R. Stephens, L. H. Conover, R. Pasternack, F. A. Hochstein, W. T. Moreland, P. P. Regna, F. J. Pilgrim, K. J. Brunings and R. B. Woodward, THIS JOURNAL, **76**, 3568 (1954).

(4) J. R. D. McCormick, N. O. Sjolander, U. Hirsch, E. R. Jensen, and A. P. Doerschuk, *ibid.*, **79**, 4561 (1957).

(5) C. R. Stephens, U. S. Patent 2,786,077, March 19, 1957.

(6) F. A. Hochstein, C. R. Stephens, L. H. Conover, P. P. Regna, R. Pasternack, P. N. Gordon, F. J. Pilgrim, K. J. Brunings and R. B. Woodward, THIS JOURNAL, **75**, 5455 (1953).

(7) A. R. English, private communication.

(8) P. Sensi, G. A. deFerrari, C. G. Gallo and G. Rolland, *Il Farmaco Ed. Sc.*, **10**, (6) 337 (1955).

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BOOK REVIEWS

The Chemistry of Organic Medicinal Products. Fourth Edition. By GLENN L. JENKINS, Professor of Pharmaceutical Chemistry and Dean of the School of Pharmacy, Purdue University; WALTER H. HARTUNG, Professor of Pharmaceutical Chemistry, Medical College of Virginia; KENNETH E. HAMLIN, Jr., Assistant Director of Chemical Research, Abbott Laboratories; and JOHN B. DATA, Associate Professor of Pharmaceutical Chemistry, The School of Pharmacy, Purdue University. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y. 1957. x + 569 pp. 16.5 × 24 cm. Price, $10.75.

The Fourth Edition has been "completely revised" but the chemical classification of medicinal agents has been retained. The number of chapters remains the same but one, "Natural Mixtures," in the Third Edition appropriately has been replaced by one on "Antibiotics." Primarily, the text is a catalogue of compounds used as medicinal agents and for other purposes (insecticides, flavoring agents). The formula, biological activity, utility (established or merely claimed), toxicity and other properties for each compound are briefly summarized. Statements concerning "activity" and "toxicity" are sometimes indefinite so that the non-expert probably will have to seek clarification elsewhere. He may sometimes wonder whether the claimed activity given for many compounds is true and the expert will question the wisdom of including some of these claims.

The chemical classification employed in the arrangement of the text provides the experienced medicinal chemist with an interesting survey of drugs from his point of view but, to the non-experienced individual or student, this grouping under a given class of a variety of compounds non-related from a drug-action point of view may have only a minimum value. For example, in Chapter 5 on Drugs Containing the Carbonyl Group (aldehydes and ketones) are found formaldehyde (disinfectant and fungicide), hexamethylenetetramine (urinary antiseptic), vanillin (flavor-