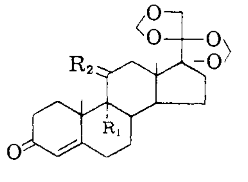
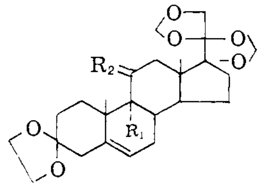
This key intermediate (IIIa) was allowed to react with methylmagnesium iodide and excess methyl iodide in refluxing ether–tetrahydrofuran. The product was chromatographically separated into 9α-methylcortisone-BMD-3-dioxolane (IIIb) [m.p. 222–228°; found C, 67.85; H, 7.51; $[\alpha]^{23}D$ −86 ± 2° ($CHCl_3$); n.m.r. showed three *tertiary* C–CH_3 groups; λ_{max}^{Nujol} 5.86, 8.8–9.3μ; rotatory dispersion curve similar to IIIc] and cortisone-BMD-3-dioxolane (IIIc).

Reduction of IIIb with lithium aluminum hydride afforded 9α-methylhydrocortisone-BMD-3-dioxolane (IIId): m.p. 230–233°; found C, 67.61; H, 7.94; λ_{max}^{Nujol} 2.7, 8.8–9.2μ. The dioxolane grouping was removed using acetone-*p*-toluenesulfonic acid to give 9α-methylhydrocortisone-BMD (IIc); m.p. 295–305°; found C, 68.40; H, 8.15; λ_{max}^{MeOH} 244 mμ, *E* 14,800; λ_{max}^{Nujol} 2.7–2.9, 5.99, 6.13, 8.8–9.4μ; R_f, *ca.* 1.3 × hydrocortisone-BMD. Reversal of the BMD function with 50% acetic acid yielded 9α-methylhydrocortisone (IVa): m.p. 220–230°; found C, 70.42; H, 8.73; λ_{max}^{MeOH} 244 mμ, *E* 14,300; λ_{max}^{Nujol} 2.8, 5.80, 6.0, 6.15 μ; 21-acetate (IVb): m.p. 235–238°; found C, 69.16; H, 8.15; λ_{max}^{MeOH} 243 mμ, *E*, 16,500; $\lambda_{max}^{CHCl_3}$ 2.9, 5.75, sh. 5.80, 6.04, 6.26, 8.2 μ.

Reaction of IVb with selenium dioxide in *t*-butanol–acetic acid produced 9α-methylprednisolone 21-acetate (IVc): m.p. 220–225°; found C, 69.02; H, 7.91; λ_{max}^{MeOH} 245 mμ, *E* 14,000; λ_{max}^{Nujol} 3.0, sh. 5.75, 5.80, 6.05, 6.18, 8.05 μ.





IIa, R_1 = Br, R_2 = $\overset{\text{OH}}{\underset{\text{H}}{<}}$

b, R_1 = Br, R_2 = O

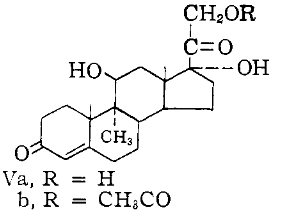
c, R_1 = CH_3, R_2 = $\overset{\text{OH}}{\underset{\text{H}}{<}}$

IIIa, R_1 = Br, R_2 = O

b, R_1 = CH_3, R_2 = O

c, R_1 = H, R_2 = O

d, R_1 = CH_3, R_2 = $\overset{\text{OH}}{\underset{\text{H}}{<}}$



IVa, R = H

b, R = CH_3CO

c, R = CH_3CO, and Δ^1 bond

In the liver glycogen test the results[5] were: IVa, about 0.1; IVb, about 0.1; IVc, about 1.6. The compounds cause slight sodium retention in adrenalectomized rats.

Acknowledgment.—The authors are indebted to Dr. L. H. Sarett for advice and encouragement during the course of this investigation.

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RECEIVED AUGUST 1, 1958

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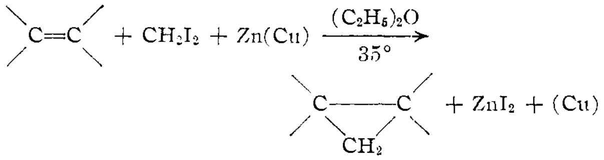
[5] Activities are expressed relative to hydrocortisone as the reference standard. We are indebted to Dr. R. H. Silber and Dr. H. C. Stoerk of the Merck Institute for Therapeutic Research for these biological tests.

A NEW SYNTHESIS OF CYCLOPROPANES FROM OLEFINS

Sir:

Although the addition of a divalent carbon intermediate to carbon–carbon unsaturation would be a direct method of forming three-membered carbocyclic rings, no completely satisfactory method for the formal addition of an unsubstituted methylene group to an olefin has been recorded. We now wish to report a versatile, stereospecific synthesis of cyclopropanes of the type I by the reaction of unsaturated compounds with methylene iodide and a zinc–copper couple.



I

Thus, cyclohexene (0.30 mole), methylene iodide (0.15 mole), and zinc–copper couple[1] (0.22 mole of zinc) were stirred at reflux in anhydrous ethyl ether for 48 hours. Simple distillation gave a 48% yield of pure bicyclo[4.1.0]heptane (b.p. 116.5°, $n^{25}D$ 1.4546),[2] whose infrared spectrum was identical to that of the authentic hydrocarbon.[3] Many functionally substituted olefins have given the corresponding cyclopropanes. Yields ranged from 10–70%, depending greatly on the kind of couple employed, and in no cases were isomeric or rearranged products encountered. Thus, ethylene, cyclopentene, bicyclo[2.2.1]hept-2-ene, 3-phenylpropene, styrene and 1-(*o*-methoxyphenyl)-propene gave cyclopropane (29%), bicyclo[3.1.0]hexane (27%), tricyclo[3.2.1.$0^{2,4}$]octane (47%), benzylcyclopropane (49%), phenylcyclopropane (32%), and 1-(*o*-methoxyphenyl)-2-methylcyclopropane (70%), respectively. Similarly, methyl crotonate and vinyl acetate afforded methyl 2-methylcyclopropanecarboxylate and cyclopropyl acetate in yields of 9 and 31%, respectively. Conditions for optimum yields have not yet been completely determined.

Ethereal solutions obtained from the reaction of zinc–copper couple and methylene iodide are known to contain iodomethylzinc iodide.[4] It is reasonable to assume that such an intermediate would undergo displacement by the π-bond of the olefin to give a cyclopropane and zinc iodide. An alternative mechanism may involve the spontaneous elimination of zinc iodide to give a low energy methylene similar in reactivity to the dihalomethylenes described by Doering and Hoffmann.[2] Either hypothesis requires stereospecificity[5] and discrimination[2,6] in the formation of a cyclopropane. This indeed was found to be the case, for when the reaction was applied to pure

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[1] F. L. Howard, *J. Research Nat. Bur. Standards*, **24**, 677 (1940).

[2] W. von E. Doering and A. K. Hoffmann, THIS JOURNAL, **76**, 6162 (1954), reported b.p. 116°, $n^{25}D$ 1.4550, for pure bicyclo[4.1.0]-heptane.

[3] We are indebted to Dr. L. H. Knox, Hickrill Chemical Research Foundation, who provided us with the infrared data on pure bicyclo-[4.1.0]heptane.

[4] G. Emschwiller, *Compt. rend.*, **188**, 1555 (1929).

[5] P. S. Skell and A. Y. Garner, THIS JOURNAL, **78**, 3409 (1956).

[6] W. von E. Doering and P. LaFlamme, *ibid.*, **78**, 5447 (1956).

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.

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[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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RECEIVED JULY 28, 1958

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.

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[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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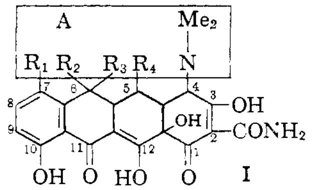
RECEIVED AUGUST 11, 1958

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).

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