der) and 1245 cm.$^{-1}$; $[\alpha]^{24}D$ +70° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{33}FO_8$: C, 62.49; H, 6.92; F, 3.95. Found: C, 62.71; H, 7.06; F, 3.63). Saponification of VIIb with sodium methoxide in methanol gave 9α-fluoro-11β,16α,17α,21-tetrahydroxy-4-pregnene-3,20-dione (VIIa), m.p. 257–260° d. (previous softening and browning); λ_{max} 238.5 mμ (ε 16,300; ν_{max} 3635, 3440, 1720, 1674 and 1630 cm.$^{-1}$; $[\alpha]^{25}D$ +91° (pyridine); *Anal.* Calcd. for $C_{21}H_{29}FO_6$: C, 63.62; H, 7.37; F, 4.79. Found: C, 63.47; H, 7.51; F, 4.49).

Microbiological dehydrogenation of VIIb with *Cornyebacterium simplex*[2e] gave after acetylation of the crude fermentation mixture 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-1,4-pregnadiene-3,20-dione (VIIIb), m.p. 158–235°[5]; λ_{max} 239 mμ (ε 15,200); ν_{max} 3390, 1740 (shoulder), 1730, 1660, 1610, 1608 (inflection) and 1235 cm.$^{-1}$; $[\alpha]^{25}D$ +22° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{31}FO_8$: C, 62.75; H, 6.53; F, 3.97. Found: C, 63.45; H, 7.44; F, 4.39). Saponification afforded the free steroid VIIIa, m.p. 260–262.5°,[6] λ_{max} 238 mμ (ε 15,800); ν_{max} 3388, 1705, 1660, 1620 and 1604 cm.$^{-1}$; $[\alpha]^{25}D$ +75° (acetone); (*Anal.* Calcd. for $C_{21}H_{27}FO_6$: C, 63.94; H, 6.90; F, 4.82. Found: C, 64.19; H, 7.17; F, 4.90).

Bio-assays:[7] In the rat liver glycogen assay (subcutaneous method) 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-4-pregnene-3,20-dione (VIIb) possessed an activity 4–8 times that of hydrocortisone; whereas, the free steroid VIIa had a 3–5 fold activity. In the same assay, 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-1,4-pregnadiene-3,20-dione (VIIIb) and its free steroid VIIIa were found to be, respectively, 15–36 and about 13 time more active than hydrocortisone.

In the rat electrolyte assay the 16α-hydroxy-fluorohydrins (VIIa,b) and 16α-hydroxy-1-dehydro-fluorohydrins (VIIIa,b) exhibited *no sodium retention properties.*

It is concluded that 16α-hydroxylation abolishes the sodium-retaining property of 9α-fluoro-steroids without destroying their glucocorticoid activity.

9α-Fluoro-11β,16α,17α,21-tetrahydroxy-1,4-pregnadiene-3,20-dione (VIIIa) and its diacetate VIIIb are the most active glucocorticoids hitherto reported which are devoid of sodium-retaining properties.

(5) The compound was apparently solvated, and the m.p. was difficult to determine. On many occasions the m.p. was about 186–188° with gas evolution.

(6) In a later run, the m.p. was 269–271°.

(7) The electrolyte assays on compounds VIIa, b were done by E. Rosenberg and R. I. Dorfman at the Worcester Foundation for Experimental Biology. These results were confirmed by P. H. Bell and F. I. Dessau and their associates (Experimental Therapeutics Research Section of these Laboratories) who also supplied the electrolyte data on compounds VIIIa,b, as well as all the glycogen data. These groups will report on their work elsewhere.

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RECEIVED OCTOBER 4, 1956

A NEW TECHNIQUE FOR THE CONVERSION OF OLEFINS INTO ORGANOBORANES AND RELATED ALCOHOLS

Sir:

In the presence of aluminum chloride the reducing powers of sodium borohydride are greatly enhanced.[1] We now wish to report that this reagent readily reacts with simple olefins, such as ethylene, 1- and 2-pentene, cyclohexene, and styrene, at temperatures of 25°, to form the corresponding trialkylboranes in yields of 90%.

Trialkylboranes are readily oxidized to the borate esters[2] which can be hydrolyzed to the corresponding alcohols. The reaction can be carried out without isolation of any of the intermediates. In this way cyclohexene has been converted into cyclohexanol, 1-hexene into 1-hexanol, styrene into 2-phenylethanol and 1,1-diphenylethylene into 2,2-diphenylethanol. The yields based on olefin are good, in the range of 70–90%. The following procedures are representative.

To a stirred solution of 0.25 mole of sodium borohydride and 0.084 mole of aluminum chloride in 250 ml. of diglyme[1] was slowly added 0.5 mole of 1-pentene. After 3 hours at room temperature, the reaction mixture was heated for 1 hour on a steam cone to complete the reaction. A nitrogen atmosphere was maintained. The flask was cooled, the diglyme removed under vacuum (<40° at 1 mm.) and the tri-*n*-pentylborane was collected at 94–95° at 2 mm. The yield was 33.0 g., 88%.

Anal. Calcd. for $C_{15}H_{33}B$: B, 4.83. Found: B, 4.55.

Oxidation by the procedure described below gave 1-pentanol of at least 95% purity, as indicated by infrared analysis. This and similar experiments indicate that in the reaction with 1-olefins, the boron becomes preferentially attached to the terminal carbon.

1,1-Diphenylethylene, 0.5 mole, was converted into the corresponding borane as described above for 1-pentene. Approximately 50% of the diglyme was removed under vacuum 1 (< 40°, 1 mm.), and the remaining solvent washed out with dilute hydrochloric acid and water. The crude product was treated with 0.2 mole of sodium hydroxide in 100 ml. of ethanol, followed by 68 g. of 30% hydrogen peroxide (20% excess) added at such a rate as to maintain a gentle reflux. The product was taken up in ether, washed and dried. Distillation gave 86.4 g. of 2,2-diphenylethanol, b.p. 192–194° at 20-mm. (87% yield). Recrystallization from petroleum ether gave a product, m.p. 64–65°, in 71% yield.

The reaction of olefins with aluminum borohydride at 140° has been reported.[3] For reasons presented earlier[1] aluminum borohydride cannot be present in the reagent in more than trace amounts. The great ease in preparing and handling the reagent as compared to aluminum borohydride should make the present procedure a highly convenient laboratory method for preparing organoboranes and for hydrating olefins. We have preliminary

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(2) J. R. Johnson and M. G. Van Campen, Jr., *ibid.*, **60**, 121 (1938).

(3) R. S. Brokaw and R. N. Pease, *ibid.*, **72**, 3237 (1950).

indications that the procedure will permit the synthesis of boranes containing certain functional groups not compatible with the Grignard reagent. We are continuing to explore the synthesis of these substances.

This investigation was assisted by grants from The Upjohn Company, Parke-Davis and Company, and Merck and Company.

DEPARTMENT OF CHEMISTRY
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RECEIVED SEPTEMBER 28, 1956

6-FURFURYLAMINO-9-β-D-RIBOFURANOSYLPURINE: SYNTHESIS AND DIFFERENTIAL TOXICITY TO MAMMALIAN CELLS *IN VITRO*[1]

Sir:

The report[2,3] that 6-furfurylaminopurine (kinetin) stimulated division of certain plant cells in tissue culture prompted the preparation of 6-furfurylamino-9-β-D-ribofuranosylpurine (I) for inclusion in a current study[4] of the effects of 6-substituted glycosyl purines on normal and neoplastic mammalian cells.

Condensation of the chloromercuri derivative of 6-methylmercaptopurine[5] with 2,3,5-tri-O-acetyl-D-ribosyl chloride followed by deacetylation gave 43% of purified 6-methylmercapto-9-β-D-ribofuranosylpurine (II). The position and configuration of the glycosyl substituent in II was established by dethiolation with Raney nickel, from which 9-β-D-ribofuranosylpurine[6] was isolated in 65% yield. Reaction of II with furfurylamine, using the method of Hitchings, *et al.*,[5] for the synthesis of amino substituted adenines, gave I, m.p. 151–152° (from methanol), in 60% yield; λ_{max}^{EtOH} 267 mμ, ϵ = 19,300; R_f 0.72 and 0.89 in *n*-butanol–water and *n*-butanol–water–acetic acid (5:3:2), respectively, (calcd. for $C_{15}H_{17}N_5O_5$: C, 51.89; H, 4.93; N, 20.16. Found[7]: C, 51.48; H, 5.05; N, 20.23).

Dr. J. Brug[8] kindly supplied a sample of a riboside (III) obtained by reaction of the chloromercuri derivative of 6-N-acetyl-furfurylaminopurine with 2,3,5-tri-O-benzoyl-D-ribosyl chloride. The m.ps. (alone or admixed), ultraviolet spectra, and paper chromatographic behavior of I and III were identical.

I exhibits an unusual differential toxicity toward fibroblasts *in vitro*.[4] In semi-synthetic medium,[9] a 1×10^{-5} *M* solution killed 99% of the cells of a strain of adult human fibroblasts in 24 hours but was almost without effect on the rate of cell division or proportion of dead cells in three strains (HeLa, H.Ep.#1 and H.Ep.#2) of human carcinoma cells. Similarly, fibroblasts of embryonic mouse skin, growing in a medium of embryo extract and serum, are more severely damaged by a 1×10^{-5} *M* solution of I than are embryonic epithelial cells or cells of mouse sarcoma 180. Studies of the usefulness of I for ridding human cancer biopsy cultures of connective tissue cells are in progress.

THE SLOAN-KETTERING DIVISION OF CORNELL UNIVERSITY MEDICAL COLLEGE NEW YORK 21, N. Y. — ALEXANDER HAMPTON, JOHN J. BIESELE, ALICE E. MOORE, GEORGE BOSWORTH BROWN

RECEIVED AUGUST 31, 1956

THE STEREOCHEMICAL CONTROL OF LEAD TETRAACETATE AND TETRABENZOATE OXIDATIONS OF CYCLOPENTADIENE

Sir:

R. Criegee,[1] some years ago, oxidized conjugated dienes with lead tetracarboxylates obtaining esters of *cis* and *trans*-glycols[2] in low yield and since then the reaction has seen only limited use.[3] Further, it has resisted interpretation. This communication establishes its ionic nature[4,5] and describes its control.

The interesting isolation,[1a] in a single instance, of a monoester (3%) of *cis*-3,4-cyclopentenediol which indicated an hydroxyl source led us to the reaction of cyclopentadiene[6] (CPD) (1.5 equivalents) and lead tetraacetate (1.0 equivalents) in glacial acetic acid containing water[4] (1.5 equivalents) at 10–20° for one half hour. There was obtained each time a mixture of monoacetates in *75–80% yield*, once distilled, b.p. 108–110° at 12 mm., $n^{25}D$ 1.123 (*Anal.* Calcd. for $C_7H_{10}O_3$: C, 59.12; H, 7.10. Found: C, 59.10; H, 6.92). Catalytic hydrogenation[1a] yielded saturated monoacetates which on *p*-nitrobenzoylation gave *cis*-1-acetoxy-2-*p*-nitrobenzoxycyclopentane in excellent yield, m.p. 96–98°, reported[7] m.p. 96–97° (*Anal.* Calcd. for $C_{14}H_{15}O_6N$: C, 57.33; H, 5.16; N, 4.78. Found: C, 57.53; H, 5.02; N, 4.79). Saponification of the saturated monoacetates and *p*-nitrobenzylation yielded *cis*-1,2-di-*p*-nitrobenzoxycyclopentane (I), m.p. 116–118°, authentic sample,[7] m.p. 116–118°, m.m.p. 116–118°. Cleavage with periodic acid indicated 93% *cis*-1,2-cyclopentanediol and yielded glutardialdehyde 2,4-dinitrophenylhydrazone (88%) m.p. 159–160°, authentic sample, m.p.

(1) This investigation was supported by funds from the American Cancer Society, Inc., the National Cancer Institute, National Institutes of Health, Public Health Service (Grant Nos. C-471, C-678(C8) and C-1355), the Atomic Energy Commission (Contract No. AT(30-1)-910), and the Damon Runyon Memorial Fund for Cancer Research.

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