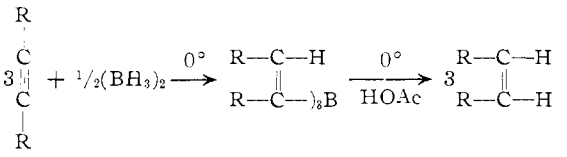
COMMUNICATIONS TO THE EDITOR

THE HYDROBORATION OF ACETYLENES—A CONVENIENT CONVERSION OF INTERNAL ACETYLENES TO CIS OLEFINS OF HIGH PURITY AND OF TERMINAL ACETYLENES TO ALDEHYDES

Sir:

The hydroboration reaction provides a convenient synthetic route for the anti-Markownikoff hydration of terminal olefins[1] and for the *cis* hydration of cyclic olefins.[2] In extending this reaction to acetylenic derivatives, we have observed that the hydroboration reaction provides a new synthetic procedure for the conversion of internal acetylenes to *cis* olefins of high purity,[3] and for the hydration of terminal acetylenes into the corresponding aldehydes.

In ether solvents internal acetylenes, such as 2-pentyne and 3-hexyne, readily undergo hydroboration to form unsaturated boron derivatives which readily are converted to the corresponding *cis* olefins by glacial acetic acid.

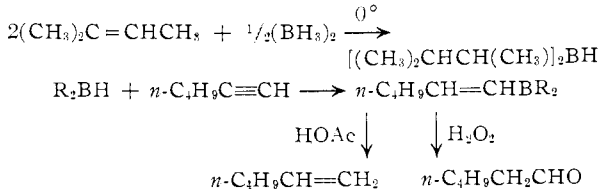


Analysis by gas chromatography (column, adiponitrile on Celite) of the *cis*-2-pentene produced in this reaction indicated it to be of remarkably high purity, approaching 100%, with only traces of the *trans* isomer suggested. Similarly, *cis*-3-hexene and *cis*-2-hexene from the corresponding acetylenes are essentially free from the corresponding *trans* isomers, both by gas chromatography (adiponitrile) and infrared examination. A minor impurity of approximately 2%, possibly the isomeric *cis* hexene, was indicated by the chromatograms.

Direct hydroboration of 1-hexyne was unsuccessful. Examination revealed that approximately half of the initial 1-hexyne had not reacted, whereas the remaining half had added two H–B bonds. To circumvent this double addition, we utilized a dialkylborane, R_2BH, with bulky alkyl groups, readily synthesized through hydroboration of 2-methyl-2-butene. In this case, the addition to 1-hexyne proceeded smoothly and 1-hexene was realized in a yield of 90%. Treatment of a similar reaction mixture with hydrogen peroxide formed *n*-hexaldehyde, isolated as the 2,4-dinitrophenylhydrazone in 88% yield. Consequently, the boron atom must add to the terminal carbon.

Similarly, treatment of 3-hexyne with this reagent (R_2BH) gives an 82% yield of *cis*-3-hexene of purity > 99%.

3-Hexyne, 24.6 g., 0.3 mole, was added to 83 ml. of a 1.00 *M* solution of sodium borohydride in diglyme. The flask was immersed in ice, flushed with nitrogen, and boron trifluoride etherate, 15.6 g., 0.11 mole, was added over a period of 1 hour. After further 30 min. at room temperature, a small quantity of ethylene glycol was added to destroy residual hydride. Then 60 ml. of glacial acetic acid was added (maintaining the nitrogen atmosphere), and the mixture left overnight at room temperature. The solution was poured into ice water, the product collected, dried, and distilled: 68% yield of *cis*-3-hexene, b.p. 67.1° at 754 mm., $n^{20}D$ 1.3957°.



Hydroboration of 2-methyl-2-butene, 33.6 g., 0.480 mole, was carried out in diglyme solution at 0° in the usual manner, utilizing 0.180 mole of sodium borohydride and 0.240 mole of boron trifluoride etherate. To the reaction product, freshly prepared, was added 1-hexyne, 16.4 g., 0.2 mole. After 30 minutes, excess hydride was destroyed with ethylene glycol. The product was oxidized at 0° with 150 ml. of 15% hydrogen peroxide, adding sufficient alkali to maintain the solution slightly alkaline (*p*H 8–9). The reaction mixture was treated with water and the aldehyde taken up in ether. An aliquot was analyzed for *n*-hexaldehyde. The 2,4-dinitrophenylhydrazone, m.p. 104°, indicated a yield of 88.5%.

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(1) H. C. Brown and B. C. Subba Rao, THIS JOURNAL, **78**, 5694 (1956); H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1936 (1957).

(2) H. C. Brown and G. Zweifel, THIS JOURNAL, **81**, 247 (1959).

(3) Diethylaluminum hydride has been utilized to reduce triple bonds to *cis* olefins: G. Wilke and M. Müller, *Ber.*, **89**, 444 (1956).

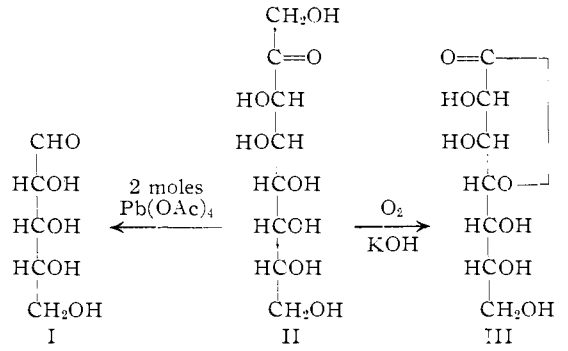
ISOLATION OF D-*glycero*-D-*manno*-OCTULOSE FROM THE AVOCADO

Sir:

In a recent examination of the aqueous extract of the fruit of the Californian avocado (Calavo; Fuerte variety) we isolated a sirupy octulose, of $[\alpha]^{20}D$ + 20° in methanol. The yield was about 1 g. of the sugar from 27 kg. of avocado. On a paper chromatogram, sprayed with the orcinol-hydrochloric acid reagent and heated in an oven at 110°, the octulose gives a crimson-colored spot that fades rapidly to gray. The octulose has been characterized by its 2,5-dichlorophenylhydrazone, m.p. 169–170° (calcd. for $C_{14}H_{20}Cl_2N_2O_7$: Cl, 17.76. Found: Cl, 17.59). Oxidation of the octulose with two molar equivalents of lead tetraacetate according to the method of Perlin and Brice,[1] and then acid hydrolysis, yielded D-ribose (I), which was identified through its crystalline *p*-

(1) A. S. Perlin and C. Brice, *Can. J. Chem.*, **34**, 541 (1956).

tolylsulfonylhydrazone.[2] Degradation of the octulose by passing oxygen through its cold solution in potassium hydroxide according to the method of Spengler and Pfannenstiel[3] yielded D-*glycero*-D-*manno*-heptonic lactone (III), which was identified by melting point, mixed melting point, rotation, and infrared spectrum through direct comparison with an authentic specimen.[4] On the basis of these degradations, the octulose must be D-*glycero*-D-*manno*-octulose (II). Its synthesis from D-*glycero*-D-*manno*-heptose[4] is now being attempted.



In addition to the octulose, we have isolated an octitol from the fruit of the Californian avocado, and are currently investigating its structure and configuration. We have obtained paper chromatographic evidence of an octulose also in the aqueous extracts of *Sedum* species and are now attempting to isolate and characterize it.

Although D-*manno*-heptulose, sedoheptulose (= D-*altro*-heptulose), and the two seven-carbon polyols perseitol and volemitol have been found in plant materials, no naturally occurring octulose or octitol has been reported previously. Racker and Schroeder[5] have shown that an octulose 8-phosphate is formed when D-ribose 5-phosphate and D-fructose 6-phosphate are incubated in the presence of a transaldolase, and it seems possible that octuloses and even higher ketoses will be discovered in trace amounts in a wide variety of plant materials.

(2) D. G. Easterby, L. Hough and J. K. N. Jones, *J. Chem. Soc.*, 3416 (1951).

(3) O. Spengler and A. Pfannenstiel, *Z. Wirtschaftsgruppe Zuckerind.*, **85**, Tech. Tl. 547 (1935).

(4) D. A. Rosenfeld, N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **73**, 4907 (1951).

(5) E. Racker and E. Schroeder, *Arch. Biochem. Biophys.*, **66**, 241 (1957).

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STEROIDAL [3,2-c]PYRAZOLES

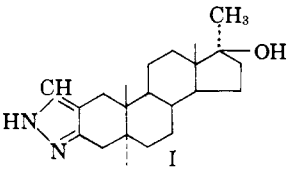
Sir:

The effect on endocrinological activity produced by the fusion of a pyrazole ring to a steroid nucleus has not been previously investigated. Only one compound of this type has been reported, *viz.*, cholest-4-eno[3,2-c]pyrazole-5′-carboxylic acid.[1]

We have found that the steroidal [3,2-c]-pyrazoles constitute a novel series of considerable endocrinological interest. Several of these compounds show a remarkable separation, or change in pattern, of hormonal activity, as well as increased oral activity, when compared to the parent steroid. The table summarizes *qualitatively* the hormonal patterns observed for a series of 17α-methyl-17β-hydroxyandrostane derivatives when tested in rats.

Compound	Estrogenic (vaginal cornification)	Androgenic (ventral prostate growth)	Myotrophic (levator ani growth)	Anabolic (nitrogen retention)
I	−	+	+	+
II	+	+	+	−
III	+	−	−	?
N-Acetyl I	+	+	+	+
N-Acetyl II	+	+	+	?

Treatment of 17α-methylandrostan-17β-ol-3-one with ethyl formate and sodium methoxide gave the 2-hydroxymethylene derivative, m.p. 185.2–190.4°, $[\alpha]_D$ +22.3°, λ_{max}. 282 mμ, E = 10,300 (found: C, 76.10; H, 9.53).[2] Condensation of the latter with hydrazine gave 17β-hydroxy-17α-methyl-androstano[3,2-c]pyrazole, I, m.p.. 229.8–242.0°,



I

$[\alpha]_D$ + 35.7°, $\lambda_{max.}$ 223 mμ, E = 4740 (Found: C, 76.65; H, 9.73; N, 8.45). Similar treatment of 2-hydroxymethylene-17α-methylandrost-4-en-17β-ol-3-one (m.p. 178.6–179.8°, $[\alpha]_D$ + 14.0°, $\lambda_{max.}$ 252,307 mμ, E = 12,000 and 6030, respectively (Found: C, 76.36; H, 9.19)) gave 17β-hydroxy-17α-methylandrost-4-eno[3,2-c]pyrazole, II, m.p. 250.0–258.0°, $[\alpha]_D$ + 133.2° (pyridine), $\lambda_{max.}$ 260 mμ, E = 11,600 (Found: C, 77.26; H, 9.31). The homologous 17β-hydroxy-17α-methylandrosta-4,6-dieno[3,2-c]pyrazole,[3] III, had m.p. 279.2–284.0°, $[\alpha]_D$ −162.1° (pyridine), λ_{max} 226, 232, 297, 308 mμ, E = 9190, 8240, 24330 and 18350 respectively (Found: C, 77.92; H, 8.53; N, 8.35).

N-Acetyl I monoethanolate, m.p. 111.4–115.4°, $[\alpha]_D$ + 43.1°, $\lambda_{max.}$ 258 mμ, E = 19000 (Found: C, 72.40; H, 9.78; N, 6.72).

N-Acetyl II ethanolate,[4] m.p. 92.0–100.2°, $[\alpha]_D$ + 67.1°, $\lambda_{max.}$ 237, 255, 289 mμ, E = 7100, 4900, 24200, respectively (Found: C, 75.20; H, 8.85; N, 7.56).

Multiple dose level oral assays (nitrogen retention in rats) indicate that I is thirty-five times more potent than methyltestosterone as an anabolic agent. On the other hand, the ventral prostate weight gain in rats indicates that I is only one-fourth as androgenic as methyltestosterone. Compound I is not

(1) L. Ruzicka and P. A. Plattner, *Helv. Chim. Acta*, **21**, 1717 (1938).

(2) Melting points are corrected; rotations are in chloroform except as noted; ultraviolet spectra are in 95% ethanol.

(3) The parent 17α-methylandrosta-4,6-dien-17β-ol-3-one has not been described previously: m.p. 196.0–197.6°, $[\alpha]_D$ +36.2°, λ_{max} 283 mμ, E = 25,990 (Found: C, 79.92; H, 9.49). The compound is predominantly anabolic in rats, but possesses weak androgenicity.

(4) A reproducible solvate, containing 15.8% ethanol. The solvent-free compound was a glass. Rotation and analyses are on a dry basis.