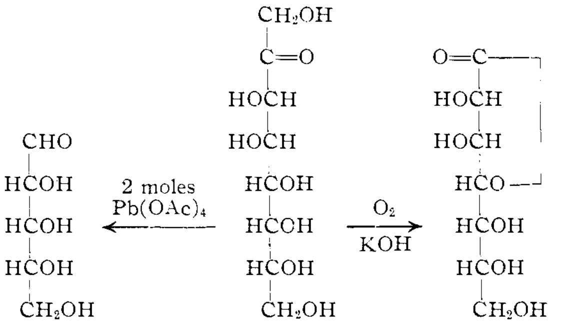
tolylsulfonylhydrazone.[2] Degradation of the octulose by passing oxygen through its cold solution in potassium hydroxide according to the method of Spengler and Pfannenstiel[3] yielded D-*glycero*-D-*manno*-heptonic lactone (III), which was identified by melting point, mixed melting point, rotation, 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.



I II III

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.

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(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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RECEIVED JANUARY 15, 1959

STEROIDAL [3,2-c]PYRAZOLES

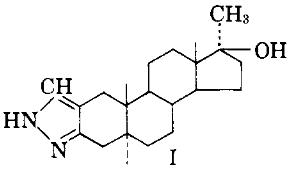
Sir:

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 corni-fication)	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°, $\lambda_{max.}$ 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

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(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.

progestational in rats or rabbits, even at high dose levels.

The unusual activity observed with the above compounds has led to the preparation of steroidal pyrazoles related to the progestational and cortical hormones, as well as to the fusion of steroids with other heterocyclic rings.

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RECEIVED FEBRUARY 10, 1959

TITANIUM TETRACHLORIDE-TRIALKYLALUMINUM COMPLEX—A CYCLIZING CATALYST FOR ACETYLENIC COMPOUNDS

Sir:

Heretofore reactions of acetylene and terminal acetylenic compounds with catalyst such as obtained from the reaction of triisobutylaluminum with titanium tetrachloride resulted only in the polymerization of these compounds to high polymers.[1] Using the same type of catalyst we have found that by regulating the ratio of $(i\text{-Bu})_3Al$ to $TiCl_4$ we can trimerize symmetrical acetylenic compounds to hexasubstituted benzenes. Thus (as shown in Fig. 1) diphenylacetylene can be trimerized to hexaphenylbenzene only between $(i\text{-Bu})_3Al/TiCl_4$ ratios of 1/1 to 3/1, although polymerization of olefins readily occurs outside these limits. Control experiments demonstrated that neither triisobutylaluminum, titanium tetrachloride, nor titanium trichloride alone could effect cyclic trimerization. In fact the $(i\text{-Bu})_3Al/TiCl_3$ polymerization catalyst does not catalyze cyclic trimerization of any acetylenes reported in this paper.

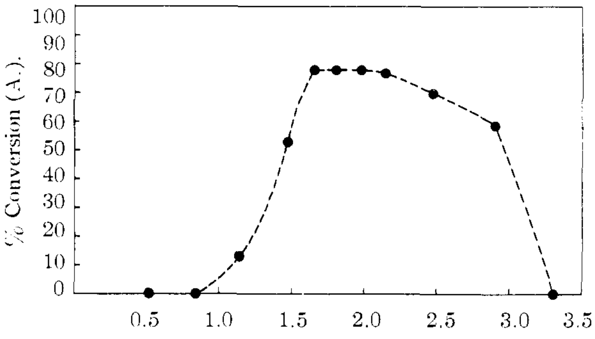


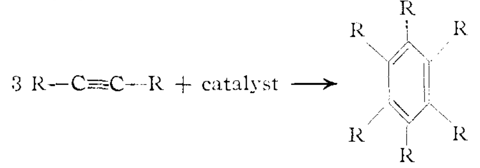
Fig. 1.—Conversion to hexaphenylbenzene *versus* mole ratio $(i\text{-Bu})_3Al/TiCl_4$: (A) conversions taken after 10 minutes at room temperature except those cases where there was 0% conversion, in which case more rigorous conditions were used after the 10 minutes had elapsed.

This type of cyclic trimerization is not limited to diphenylacetylene. Any symmetrical dialkyl or diarylacetylene will trimerize at the proper catalyst ratio. Dimethylacetylene trimerizes to hexamethylbenzene in 100% yield at $(i\text{-Bu})_3Al/TiCl_4$ ratios of 1.8/1. The "crude" product melted at 161–162° compared to 162° obtained by Smith and Lux[2] after recrystallization. One hundred per cent. yields of hexaethylbenzene (m.p. "crude" product 127–128° compared to 126–128° obtained by Smith and Guss[3] after recrystallization) were obtained from diethylacetylene using the $(i\text{-Bu})_3Al/TiCl_4$ catalyst. Seventeen moles of cyclic trimer per mole of catalyst were obtained, indicating the "catalytic" nature of this reaction.

Identities of the hexasubstituted benzenes were established by comparison of infrared spectra with those of authentic samples. Hexamethylbenzene and hexaethylbenzene were available but hexaphenylbenzene was synthesized[4] by condensation of diphenylacetylene[5] with tetraphenylcyclopentadienone. The infrared and X-ray spectra of the authentic and unknown samples were identical.

Recently, using organometal compounds, Zeiss[6] has obtained cyclic trimers of two acetylenic compounds. The organometal compound was used in stoichiometric amounts, rather than in the small quantities normally considered as catalytic amounts, and the reaction has required specific organometal compounds for specific symmetrical acetylenes. Nevertheless, the similarity of products obtained from Zeiss' systems and the $(i\text{-Bu})_2Al/TiCl_4$ system might reflect a relationship between the two which will provide a valuable clue to the $(i\text{-Bu})_3Al/TiCl_4$ catalyst structure.

In summary, the catalytic system $(i\text{-Bu})_3Al/TiCl_4$ previously believed applicable only to the polymerization of olefins (or acetylenes) to form high polymers can now be used for cyclic trimerization of disubstituted acetylenes in the completely general reaction



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[1] (a) G. Natta, P. Pino and G. Mazzanti, Belgian Patents 546,151, Mar. 16, 1956; (b) 548,927, June 22, 1956.

[2] L. I. Smith and A. R. Lux, THIS JOURNAL, **51**, 2997 (1929).

[3] L. I. Smith and C. O. Guss, *ibid.*, **62**, 2625 (1946).

[4] W. Dilthey and G. Hurtig, *Ber.*, **67B**, 495, 2005 (1934).

[5] L. I. Smith and M. M. Falkof, *Org. Syn.*, **22**, 50 (1942).

[6] (a) H. H. Zeiss and W. Herwig, THIS JOURNAL, **80**, 2913 (1958); (b) M. Tsutsui and H. Zeiss, p. 59-P, Abstracts of Papers, 134th Meeting American Chemical Society, September 7–12, Chicago, Illinois.

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RECEIVED OCTOBER 6, 1958

PARTIAL ASYMMETRIC SYNTHESIS IN THE ADDITION OF DIPHENYLDIAZOMETHANE TO OLEFINS[1]

Sir:

Cram and Abd Elhafez[2] and Prelog and coworkers[3,4] have studied the course of asymmetric syntheses in a number of systems and have found

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[1] This work was supported by a grant from the National Science Foundation.

[2] D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5828 (1952).

[3] V. Prelog, *et al.*, *Helv. Chim. Acta*, **36**, 308 (1953).

[4] For a review of this work, see J. A. Mills and W. Klyne, Ch. 5 in "Progress in Stereochemistry," Vol. I, Academic Press Inc., New York, N. Y., pp. 198–201.