

doubtedly reflected in the transition state leading away from XVI and will also be evident at least initially in an ion pair derived from XVI. The results of the above experiments and other unpublished studies indicate that in rearrangements of substances like I, the role of A varies and this depends to a large degree on the nature of the cation, the solvent, etc. It appears that it will not be possible to write a general structure for these intermediates but rather that each case will have to be investigated in its own right.

### Experimental

**Benzoic Acid-CO<sup>18</sup>O<sup>18</sup>H (IV).**—A mixture of 74.0 g. (0.379 mole) of benzotrichloride and 25 ml. of H<sub>2</sub>O<sup>18</sup> (ca. 1.5 atom % oxygen-18) was heated with stirring on a steam-bath for 24 hr. The resulting solid was filtered and dried to afford 43.0 g. (93%) of benzoic acid, m.p. 118–119°. The acid was recrystallized from benzene-hexane to yield 40.3 g. of material, m.p. 123–124°.

**Benzoyl Chloride-CO<sup>18</sup>Cl (V).**—A mixture of 13.0 g. (0.1075 mole) of I and 20 ml. of thionyl chloride was allowed to stand at room temperature for 24 hr. The thionyl chloride was removed *in vacuo* and the product was distilled to yield 13.9 g. (93%) of II, b.p. 88–89° (20 mm.).

**trans-9-Decalyl Perbenzoate-carbonyl-O<sup>18</sup> (VI).**—VI was prepared in 72% yield, m.p. 66–66.8° (lit.<sup>9</sup> 67–68°), by the method of Cope and Holtzman.<sup>9</sup>

**Labeled 1-Benzoyloxy-1,6-epoxycyclodecane (Xa).**—VI was allowed to rearrange in methanol according to the procedure of Bartlett and Kice.<sup>4</sup> An 85% yield of IV was obtained, m.p. 96.7–97° (lit.<sup>9</sup> 96.5–97.5°), after crystallization from methanol-water.

**Labeled 1-Benzoyloxy-1,6-epoxycyclodecane (Xb).**—VI was allowed to rearrange in glacial acetic acid for 22 hr. at 21°. An 80% yield of Xb, m.p. 94.5–95.5°, was obtained after crystallization from methanol-water.

**Reduction of Xa and Xb.**—To a stirred suspension of 2.0 g. (0.0526 mole) of lithium aluminum hydride in 50 ml. of ether was added 4.34 g. (0.0158 mole) of Xb in 100 ml. of dry ether. The mixture was stirred and refluxed for 24 hr. After cooling to 0°, water was added and the ether layer was separated from the solid and water. The dried solid was

extracted in a Soxhlet with chloroform. The chloroform extract was evaporated to give a solid which was recrystallized from acetone to yield 1.92 g. (71%) of XIb, m.p. 140.6–142.6°.

*Anal.* Calcd. for C<sub>10</sub>H<sub>20</sub>O<sub>2</sub>: C, 69.72; H, 11.70. Found: C, 70.04; H, 11.60.

The original ether extracts were dried over magnesium sulfate. The ether was evaporated and the residue was distilled in a molecular still, block temperature 100–110° (20 mm.). One main fraction, 0.70 g. (41%), *n*<sub>D</sub><sup>20</sup> 1.5378, was obtained. The infrared spectrum of this sample agreed with that of a known sample of benzyl alcohol.

In a similar manner Xa was reduced to XIa and XIIa. The phenylurethans of XIIa and b were prepared by standard methods, m.p.'s 77–78°.

**p-Nitrobenzoic Acid-CO<sup>18</sup>O<sup>18</sup>H (XIII).**—To a solution of 60.0 g. of H<sub>2</sub>O<sup>18</sup> (1.5 atom % oxygen-18) in 500 ml. of dry tetrahydrofuran there was added 185 g. (1.00 mole) of *p*-nitrobenzoyl chloride. The solution was refluxed for two days. The solvent was evaporated and the crude acid was crystallized from methanol, m.p. 240–242°.

**p-Nitrobenzoyl Chloride-CO<sup>18</sup>Cl (XIV).**—A mixture of 300 ml. of thionyl chloride and 80.0 g. (0.431 mole) of XIII was refluxed for 8 hr. The thionyl chloride was removed *in vacuo* and the acid chloride was recrystallized from hexane to yield 56.5 g. (63%) of XIV, m.p. 71.5–72°.

The amide was prepared by standard procedures, m.p. 200–201°.

**p-Nitro-*p*'-methoxybenzoyl Peroxide-*p*-nitrobenzoyl-carbonyl-O<sup>18</sup> (XVI).**—The procedure of Leffler<sup>6</sup> was followed exactly. The yield was 13% of material, m.p. 114° dec. (lit.<sup>6</sup> 108°).

**Labeled p-Nitrobenzoyl-*p*-methoxyphenyl Carbonate (XVII).**—The peroxide XVI was rearranged as reported by Leffler.<sup>6</sup> The yield was 40% of material, m.p. 123–124° (lit.<sup>6</sup> 126–129°).

**Labeled p-Nitrobenzamide (XVIII).**—The carbonate XVII, 0.80 g. (0.00252 mole), was added to 20 ml. of liquid ammonia at –33°. The mixture was stirred and the ammonia was allowed to evaporate. The solid residue was washed with 5% sodium hydroxide solution. The amide was recrystallized from methanol to yield 0.20 g. (48%) of XVIII, m.p. 200–201°, no depression with an authentic sample.

(9) A. C. Cope and G. Holtzman, *THIS JOURNAL*, **72**, 3062 (1950).

NEW BRUNSWICK, N. J.

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## COMMUNICATIONS TO THE EDITOR

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### STEROIDAL LACTONES

Sir:

We wish to report the preparation of two steroids, III and V, which significantly reverse the electrolytic effects of mineralocorticoids.

Treatment of 17 $\alpha$ -ethynyl-5-androstene-3 $\beta$ ,17 $\beta$ -diol<sup>1</sup> with ethylmagnesium bromide in tetrahydrofuran, followed by carbonation with gaseous carbon dioxide yielded, upon hydrolysis, 3 $\beta$ ,17 $\beta$ -dihydroxy-5-androsten-17 $\alpha$ -ylpropionic acid (I)<sup>2</sup>, m.p. 234–235° (dec.), [ $\alpha$ ]<sub>D</sub> –132.5° (diox.); *Anal.* Calcd. for C<sub>22</sub>H<sub>30</sub>O<sub>4</sub>·H<sub>2</sub>O: C, 70.18; H, 8.57. Found: C, 70.19; H, 8.46. Saturation of the triple bond by hydrogenation in ethanol with palladium on carbon catalyst afforded 3-(3 $\beta$ ,17 $\beta$ -dihydroxy-5-androsten-17 $\alpha$ -yl)-propionic acid  $\gamma$ -lactone (II),<sup>2</sup> m.p. 190–191°, [ $\alpha$ ]<sub>D</sub> –91.5° (CHCl<sub>3</sub>); *Anal.*

Calcd. for C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>: C, 76.70; H, 9.36. Found: C, 76.40; H, 9.90. Oppenauer oxidation of II yielded 3-(3-oxo-17 $\beta$ -hydroxy-4-androsten-17 $\alpha$ -yl)-propionic acid  $\gamma$ -lactone (III),<sup>2</sup> m.p. 148–150° (163–165°), [ $\alpha$ ]<sub>D</sub> +76.5° (CHCl<sub>3</sub>); *Anal.* Calcd. for C<sub>22</sub>H<sub>30</sub>O<sub>3</sub>: C, 77.15; H, 8.83. Found: C, 77.31; H, 8.94.

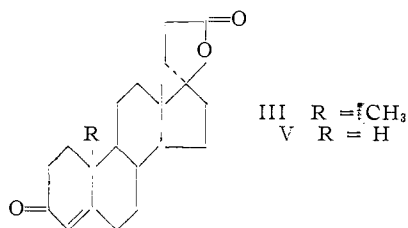
The 19-nor analog of III was prepared. The Grignard reagent of 3-methoxy-17 $\alpha$ -ethynyl-1,3,5-(10)-estratrien-17 $\beta$ -ol<sup>3</sup> was prepared in tetrahydrofuran and carbonated with gaseous carbon dioxide. There was obtained upon hydrolysis 3-methoxy-17 $\beta$ -hydroxy-1,3,5(10)-estratrien-17 $\alpha$ -ylpropionic acid monohydrate (IV), m.p. 204–207° dec. (–H<sub>2</sub>O 120–140°), [ $\alpha$ ]<sub>D</sub> –17.7° (diox.) *Anal.* Calcd. for C<sub>22</sub>H<sub>26</sub>O<sub>4</sub>·H<sub>2</sub>O: C, 70.94; H, 7.58. Found: C, 70.74; H, 7.93. The acid hydrate IV was suspended in ammonia and ethanol and treated

(1) H. E. Stavelly, *THIS JOURNAL*, **61**, 79–80 (1939).

(2) J. A. Cella, U. S. Patent 2,705,712, April 5, 1955.

(3) F. B. Colton, U. S. Patent 2,666,769, Jan. 19, 1954.

with metallic lithium<sup>4</sup> thereby causing reduction of both the triple bond and the aromatic A ring. Hydrolysis with mineral acid followed by chromatography yielded 3-(3-oxo-17 $\beta$ -hydroxy-19-nor-4-androsten-17 $\alpha$ -yl)propionic acid  $\gamma$ -lactone (V), m.p. 126.5–127° (137–138°),  $[\alpha]_D^{25} +22.7^\circ$  (CHCl<sub>3</sub>); *Anal.* Calcd. for C<sub>21</sub>H<sub>28</sub>O<sub>3</sub>: C, 76.79; H, 8.59. Found: C, 76.49; H, 8.34.



Bioassay<sup>5</sup>—reversal of the effect of desoxycorticosterone (DOC) on the urinary Na–K ratio of adrenalectomized rats was used as a measure of potency. If progesterone, recently described as capable of reversing the effect of DOC,<sup>6</sup> is assigned an activity of 1, then III and V were found to have an activity of approximately 8 and 27, respectively. In similar tests III and V also reversed the electrolyte effects of aldosterone.

(4) A. L. Wilds and N. A. Nelson, *THIS JOURNAL*, **75**, 5360 (1953).

(5) The details of bioassay will be reported elsewhere.

(6) R. L. Landau, D. M. Bergenstal, K. Lugibihl, and M. E. Kaschl, *J. Clin. Endocrinol. and Metabolism*, **15**, 1194 (1955).

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RECEIVED JULY 24, 1957

#### CYCLIZATION IN GAMMA RAY IRRADIATED HIGH DENSITY POLYETHYLENE

Sir:

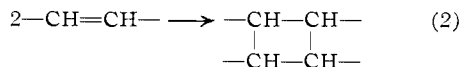
Material balance in the irradiation of polyethylene has never been convincingly attained, especially at liquid nitrogen temperatures where  $G(H_2)$  and  $G(-CH=CH-)$  are essentially equal to their values at room temperature while cross link formation is sharply reduced.<sup>1</sup>

As adapted to the high density polyethylene, Marlex-50, and considering no chain scission, the material balance equation can be written

$$[H_2] + [Vi^0 - Vi] = \frac{1}{2}[R] + [VI] + [C.L.] + [E.L.] + [S.L.] + [R.L.] \quad (1)$$

where brackets signify moles per gram of substances produced during the irradiation except for  $Vi^0 - Vi$  which represents moles/g. of vinyl groups destroyed. R, VI, C.L., E.L., S.L. and R.L. signify free radicals, vinylene groups, cross, end,<sup>2</sup> square and ring links, respectively.

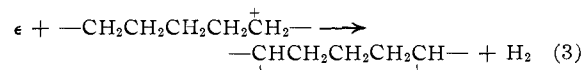
By "square" links we mean double cross links formed by a reaction such as



(1) A. Charlesby and W. H. T. Davison, *Chem. and Ind.*, 232 (1957).

(2) A. Charlesby has proposed the term "end link," *Proc. Roy. Soc.*, **A231**, 521 (1955).

Such a square link is assumed in Eq. (1) to constitute one cross link as well as one square link. By "ring" links we mean intramolecular bonds formed by reactions such as



( $\epsilon$  represents the electron). Equation (3) is similar to a reaction proposed earlier.<sup>3</sup> Other ring forming reactions could be proposed.

Cross links and vinylene groups formed by irradiation have been recognized since 1950,<sup>3</sup> but ring or square links have never before been observed in the irradiation of any substance as far as we know. It is the purpose of this note to present evidence for cyclization during irradiation.

1,2-Disubstituted cyclopentane and cyclohexane derivatives absorb<sup>4</sup> in the infrared approximately at wave lengths of 10.2  $\mu$  with extinction coefficients varying between 6 and 28 l. cm<sup>-1</sup>. mole<sup>-1</sup>. In Marlex-50 the initial absorption at 10.0 and 10.98  $\mu$  due to the vinyl group rapidly falls with irradiation at room temperature and *in vacuo* (initial  $G(-vinyl)$  equal to 7.7), revealing the growth of another absorption at 10.1  $\mu$  which is approximately the wave length at which *trans* 1,2-disubstituted cyclopentanes and hexanes absorb. We have attributed the growth of this peak to the formation of ring links of this size (other ring or square links which might absorb at this wave length are not excluded). A similar growth in the peak at 10.1  $\mu$  was found also in the case of a Ziegler-type polyethylene.

An order of magnitude estimate of  $G$  (*trans* ring links) is 1.0 which is of sufficient magnitude to show the necessity of considering cyclization in attempting to achieve a material balance.

In the case of a low density polyethylene, the vinylene peak at 10.3  $\mu$  is broader than in the case of Marlex-50 and possibly obscures the peak due to the ring systems. The 10.3  $\mu$  peak is unsymmetrical, however, which suggests that ring links are produced in low as well as high density polyethylenes.

This research was supported by a grant from the U.S. Atomic Energy Commission.

(3) M. Dole, Report of Symposium IV, "Chemistry and Physics of Radiation Dosimetry," Army Chemical Center, Md., September, 1950.

(4) "Catalog of Infrared Spectral Data" of the American Petroleum Institute Research Project, Carnegie Institute of Technology, Pittsburgh, Pennsylvania.

(5) Fulbright Fellow, 1956.

(6) On leave from A.E.R.E., Harwell, England.

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RECEIVED JUNE 17, 1957

#### ENZYMATIC OXYGEN FIXATION INTO ACETATE CONCOMITANT WITH THE ENZYMATIC DECARBOXYLATION OF L-LACTATE

Sir:

The enzymatic incorporation of molecular oxygen into various organic substrates recently has been