sized this ketone by the application of the Oppenauer oxidation[2] on β-ionylidene ethyl alcohol (I) which was prepared by the reduction of ethyl β-ionylidene acetate with lithium aluminum hydride.[3,4]

Ethyl β-ionylidene acetate (b. p. 141–144° (2–3 mm.); $n^{25}D$ 1.5320; $\lambda_{max.}$ 2850 Å., log ε 4.42) was prepared according to Karrer, *et al.*,[5] by the Reformatsky condensation of β-ionone ($n^{25}D$ 1.5180) and ethyl bromoacetate. The intermediate hydroxy ester was dehydrated with *p*-toluene sulfonic acid in toluene. This ester (180 g.) was reduced in an ethereal solution at 0° with lithium aluminum hydride (32 g.) prepared essentially by the recently published method.[3] The product (163 g.) was recovered after acidification with a mixture of ice and glacial acetic acid and fractionated under reduced pressure and the fraction (113.6 g.) boiling at 137–144° (4 mm.), collected and analyzed; $n^{25}D$ 1.5496; $\lambda_{max.}$ 2740 Å., log ε 4.45.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98; unsaturation, 3 ⌐; active hydrogen, 1.0. Found: C, 81.42; H, 10.92; unsaturation, 3.12, 3.17 (Pt) ⌐; active hydrogen (Zerewitinoff), 0.99, 1.01, 1.02.

β-Ionylidene ethyl alcohol (44.8 g.) was dissolved in a mixture of thiophene-free benzene (1000 cc.) and purified acetone (400 cc.) and to the mixture was added 60 g. of freshly prepared aluminum *t*-butoxide and refluxed in nitrogen for forty-four hours. The mixture was cooled, hydrolyzed with 1 liter of water and filtered and the benzene layer separated from the filtrate, dried and the benzene removed under vacuum; yield of the crude product, 40 g. (active hydrogen, 0.55). This dark brown product was distilled under a high vacuum and the fraction (32 g.) distilling at 80–85° (10^{-4}–10^{-5} mm.) collected and analyzed. Carbon and hydrogen showed the presence of about 10% ketol, so that the product was further dehydrated with 2% *p*-toluene sulfonic acid in toluene. The ketone was recovered and, after preliminary purification in petroleum ether and in methanol at −78°, was fractionated under high vacuum and the fraction (yellow oil, 24.5 g.) boiling at 80–82° (10^{-4}–10^{-5} mm.) was collected and analyzed; $n^{17}D$ 1.5685; $\lambda_{max.}$ 3330 Å., log ε 4.2.

Anal. Calcd. for $C_{18}H_{26}O$: C, 83.67; H, 10.14; unsaturation, 4.0 ⌐. Found: C, 83.67; H, 10.43; unsaturation, 4.15 ⌐.

The ketone had a negligible active hydrogen (Zerewitinoff) and gave a wine red color with antimony trichloride in chloroform. We expect to carry out a Reformatsky on this ketone, dehydrate the hydroxy ester and reduce the final ester to vitamin A with lithium aluminum hydride.

(2) Batty, Burawoy, Harper, Heilbron and Jones, *J. Chem. Soc.*, 175 (1938).

(3) Finholt, Bond and Schlesinger, THIS JOURNAL, **69**, 1199 1947).

(4) Nystrom and Brown, *ibid.*, **69**, 1197 (1947).

(5) Karrer, Salomon, Morf and Walker, *Helv. Chim. Acta*, **15**, 878 (1932); Karrer, Morf and Schoepp, *ibid.*, **16**, 557 (1933); Karrer, Ruegger and Solmssen, *ibid.*, **21**, 448 (1938).

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RECEIVED AUGUST 26, 1947

PHOSPHITE ISOMERIZATION IN THE SYNTHESIS OF THIOPHENE PHOSPHONIC ACIDS

Sir:

In view of the very poor yields heretofore attainable in the preparation of thiophene-substituted phosphonic acids,[1] the classical isomerization of alkylphosphites was tried in an attempt to make the compounds of this type more available for study.

Sodium dibutylphosphite (from 45 g. of dibutyl phosphite) was treated in hexane solution with 31 g. of α-chloromethylthiophene to give, after three hours of reflux, 71% yield of dibutyl α-thienylmethanephosphonate, b. p. 147–150° at 3 mm. Hydrolysis by boiling with hydrochloric acid, followed by evaporation and recrystallization of the residue from water, gave a substantially quantitative conversion of the ester to α-thienylmethanephosphonic acid, which formed yellowish plates; m. p. 108–109°. *Anal.* Calcd.: S, 16.3. Found: S, 16.46.

(1) Sachs, *Ber.*, **25**, 1514 (1892).

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CARCINOGENESIS

Sir:

Concerning the excellent paper by L. F. Fieser and S. T. Putnam on the Oxidation of Carcinogenic Hydrocarbons in the May issue of THIS JOURNAL, I should like to suggest that peroxidation is more important than oxidation in determining their carcinogenicity. Since the ionization potential decreases with the number of conjugation centers, a simple electron transfer process involving the non-localized π electrons can readily occur with these hydrocarbons. This may be followed by a proton transfer resulting in the formation of a free-radical. This radical reacts with oxygen to form a peroxide free-radical capable of initiating a branched-chain, free-radical oxidation of intracellular nutrient material, thus increasing cell-metabolism and cell-growth. In the presence of trace quantities of such materials as chromium, iron, cobalt, arsenic, ascorbic acid, etc., the activation energy required for the decomposition of the hydroperoxides into free radicals may be low enough to accelerate tissue growth to the extent that it is entirely out of proportion to the growth rate of the normal surrounding tissues.

The hydroperoxides will increase until limited by the supply of arterial oxygen. Since they are a