This fact suggested that similar rearrangements might be observed in the Grignard reactions of isotope-labeled 3-butenyl halides. Indeed, when the Grignard reagent prepared from the ^{14}C-labeled chloride IV[3] was oxygenated some 24 hours after formation, *equal amounts* of the normal (V) and rearranged[4] (VI) alcohols were formed.

$$\underset{\text{IV}}{CH_2{=}CHCH_2{}^{14}CH_2Cl} \xrightarrow[3.\ H_2O]{1.\ Mg;\ 2.\ O_2} \underset{\text{V}}{CH_2{=}CHCH_2{}^{14}CH_2OH} + \underset{\text{VI}}{CH_2{=}CH{}^{14}CH_2CH_2OH} \quad (2)$$

These results are consistent with the intervention of cyclopropylcarbinyl intermediates somewhere between formation of the Grignard reagent and the final products. Product analysis alone does not establish at which stage(s) rearrangement occurs. Nuclear magnetic resonance (n.m.r.) spectroscopy, however, has been decisive in determining the structures of the carbon radicals of the Grignard reagents and in demonstrating that it is only the reagents themselves which rearrange (Eq. 3), there being no detectable rearrangement during their formation or reaction.

First, n.m.r. spectra clearly show that $\gtrsim 99\%$ of the Grignard reagent from allylcarbinyl chloride (or bromide) has the allylcarbinyl structure. Furthermore, the observation of two discrete aliphatic CH_2 resonances (separation 163.3 cps.) implies that the mean lifetimes of VII and IX are

$$\underset{\text{VII}}{CH_2{=}CHCH_2{*}CH_2MgX} \rightleftharpoons \underset{\text{VIII}}{{*CH_2}\diagdown\!\!\diagup CHCH_2MgX} \rightleftharpoons \underset{\text{IX}}{CH_2{=}CH{*}CH_2CH_2MgX} \quad (3)$$

a, $*CH_2 = CH_2$, X = Cl
b, $*CH_2 = {}^{14}CH_2$, X = Cl
c, $*CH_2 = CD_2$, X = Br

$\geq 10^{-2}$ sec.[5] Second, the n.m.r. spectrum of the Grignard reagent prepared from cyclopropylcarbinyl chloride shows only the allylcarbinyl structure, as might be expected from prior chemical evidence that this reagent affords exclusively allylcarbinyl products.[6]

An n.m.r. study of the rearrangement of 3-butenyl-1,1-$^2H_2$-magnesium bromide (VIIc) to 3-butenyl-2,2-$^2H_2$-magnesium bromide (IXc) in concentrated ethereal solution and of the products of oxygenation and of carbonation of VIIc has demonstrated unequivocally that the Grignard reagent rearranges after its formation and prior to conversion to final products. The Grignard reagent prepared from 3-butenyl-1,1-$^2H_2$ bromide[7] was 97% VIIc[8] as evidenced by the relative areas of the CH_2 doublet at 7.82 (VIIc) and singlet at 10.54 (IXc) (*cf.* Fig. 1). When the Grignard solution is allowed to stand, VIIc is converted slowly to IXc and, at equilibrium, the characteristic CH_2 peaks of each have equal areas (Fig. 1). The half-times for equilibration are thirty hours at 27° and forty minutes at 55.5°, corresponding to an activation energy of about 23 kcal.

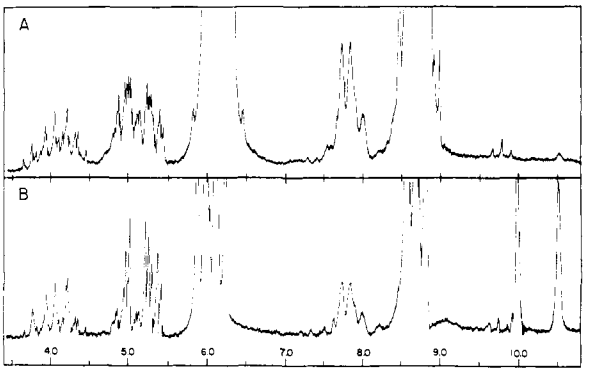

Fig. 1.—N.m.r. spectra at 60 mc.: curve A is VIIc and curve B is VIIc + IXc at equilibrium. B shows the internal standard, $Si(CH_3)_4$ (≡10.00 τ units). The ether bands are 6.1 (CH_2), 8.7 (CH_3) and 9.8 ($^{13}CH_3$).

The n.m.r. spectra of the products isolated after oxygenation and carbonation of VIIc (at least 97% pure[8]) showed no evidence of further rearrangement as judged by location and areas of the CH_2 peaks and of the multiplet structure of the vinyl lines.

The details of these and other results regarding the interconversion of allylcarbinyl and cyclopropylcarbinyl Grignard reagents will be published later.

(3) Prepared from 3-butenonitrile-1-^{14}C (allyl bromide and cuprous cyanide-^{14}C) by hydrolysis, hydride reduction and reaction with thionyl chloride.

(4) The product ^{14}C distribution was determined by conversion to butyric acid and then Curtius rearrangement to the isocyanate, which with phenylmagnesium bromide gave N-propylbenzamide, the ^{14}C activity of which (0.0418 ± 0.0003 mc./mmole) was taken as 100%. Hydrolysis gave benzoic acid (0.0205 ± 0.0002 mc./mmole) and *n*-propylamine (0.0206 ± 0.0002 mc./mmole as N-propylbenzamide). Successive oxidations of the labeled allylcarbinol with performic acid and periodate gave formaldehyde (C-4) with no ^{14}C activity.

(5) *Cf.* J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Company, New York, N. Y., 1959, Chap. IV; compare with allylmagnesium bromide, J. E. Nordlander and J. D. Roberts, THIS JOURNAL, **81**, 1769 (1959).

(6) J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 2509 (1951).

(7) Prepared from methyl 3-butenoate by deuteride reduction and conversion of the deuterioalcohol to the bromide via the benzenesulfonate and reaction with lithium bromide. The purity of both the alcohol and the bromide was determined by n.m.r. and vapor-phase chromatography to be >98.5%.

(8) The preparation and concentration of the n.m.r. sample at 20° required about six hours; consequently, on the basis of the rate data above, it is likely that no rearrangement takes place in the reaction of the halide with magnesium.

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PHOSPHONITRILIC BROMIDES[1]

Sir:

The paucity of available information on the bromine analogs of the phosphonitrilic chlorides probably is due to the general beliefs that substantial thermal decomposition of phosphorus-

(1) This research was supported by Contract AF 33(616)5486 with the Materials Laboratory of Wright Air Development Center, Wright-Patterson Air Force Base, Ohio.

(V) bromide at the temperature necessary for synthesis (*ca.* 100°) keeps the yield very low and that separation of the trimer and tetramer is very difficult to achieve.[2-5] We have found, however, that under proper conditions, phosphorus(III) bromide, bromine, and ammonium bromide react in *sym*-tetrachloroethane or *sym*-tetrabromoethane to yield the mixed phosphonitrilic bromides in yields as high or higher than the best reported for the chlorides.[6] To some extent, the latter solvent is the less effective since it suffers partial conversion to pentabromoethane.

In a typical reaction, 350 g. of bromine was added over a period of 4 days to a mixture of 300 g. of phosphorus(III) bromide and 250 g. of ammonium bromide in 450 ml. of *sym*-tetrachloroethane maintained at 110–120°. The temperature was then increased slowly and the mixture was held at 145–155° for 2–3 days. After cooling, the unused ammonium bromide was removed by filtration, and the solvent was evaporated (35–40° at 2 mm.). The resulting crude product was separated from oily homologs and sublimed *in vacuo* (130–160° at 0.05–0.5 mm.) to recover the trimeric and tetrameric phosphonitrilic bromides. The yield was 112.5 g., or 50%.[7] The trimer is present in considerably greater quantity than the tetramer.

However, if *sym*-tetrabromoethane is used as solvent and the temperature is increased, the tetramer predominates. Thus with the same quantities of reagents but with the temperature maintained at 160–175° for several days after addition of the bromine, 58.5 g. (25.7% of theoretical) of sublimed phosphonitrilic bromide containing over 50% of the tetramer was obtained, together with larger quantities of the higher homologs and some 30 g. of pentabromoethane.

Fractional sublimation was used to effect gross separation into trimer-rich (90–100° at 0.025 mm.) and tetramer-rich (130–150° at 0.025 mm.) fractions. Final separation then was achieved by chromatography using an aluminum oxide column or fractional crystallization from organic solvents.

Reaction in either solvent at still higher temperatures converts increasing quantities of the lower polymers to rubber-like substances comparable in appearance and properties to the phosphonitrilic chloride rubbers. At above 350°, these materials lose their elasticity, become brittle, and become quite stable toward boiling acids or alkalies.

In the chloride system, the monomeric adduct $PNCl_2 \cdot PCl_5$ has been obtained only by treating the trimer with phosphorus(V) chloride at 250° in a sealed tube or by allowing phosphorus(III) chloride to react with tetrasulfur tetranitride.[8] In the bromide system, the corresponding adduct $PNBr_2 \cdot PBr_5$ is isolated easily by stopping the reaction after addition of bromine and while the system is still at the lower temperature. Rapid removal of ammonium bromide by filtration, followed by cooling the remaining brown solution to 0°, gives large quantities of the crystalline, orange compound.

Anal. Calcd. for P_2NBr_7: N, 2.21; P, 9.75; Br, 88.04. Found: N, 2.41; P, 10.29; Br, 89.39.

This adduct is more stable than phosphorus(V) bromide, but it decomposes slowly on standing and hydrolyzes within a matter of minutes in water. It is insoluble in the ordinary organic solvents, but phosphorus(V) oxytrichloride, bromoform, *o*-dichlorobenzene, *sym*-tetrachloroethane, and *sym*-tetrabromoethane dissolve it with decomposition. The compound gives a distinctive X-ray diffraction pattern. When heated in *sym*-tetrachloroethane, it polymerizes to small quantities of the trimer and tetramer and large quantities of the higher homologs.

Solubility, infrared, nuclear magnetic resonance, X-ray diffraction, and chemical data will be discussed in a subsequent paper.

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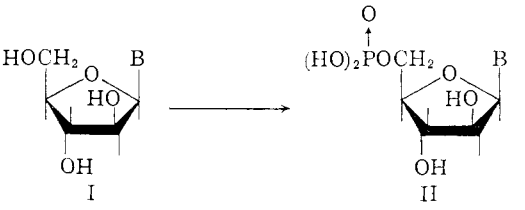
POTENTIAL ANTICANCER AGENTS.[1] XL. SYNTHESIS OF THE β-ANOMER OF 9-(D-ARABINOFURANOSYL)-ADENINE

Sir:

Recent studies by Pizer and Cohen[2] have shown some unique, highly surprising, and very useful substrate properties of 1-(β-D-arabinofuranosyl)-uracil (I, B = uracil). This compound is phosphorylated to the nucleotide (II, B = uracil) by the enzyme that phosphorylates deoxyuridine *but not uridine*. Secondly, II (B = uracil) is methylated to the thymine nucleotide (II) by the enzyme that converts deoxyuridylic acid to thymidylic acid, an enzyme that will *not* methylate



uridylic acid. Finally, nucleoside phosphorylase will not rupture the arabinosyl-uracil bond under conditions in which the ribosyl and deoxyribosyl nucleosides of uracil are cleaved,[2] in contrast to its action on the important anticancer agent, 5-

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. SA-43-ph-1892. The opinions expressed in this paper are those of the authors and are not necessarily those of the Cancer Chemotherapy National Service Center. For the preceding paper in this series, *cf.* A. Benitez, O. P. Crews, Jr., L. Goodman and B. R. Baker, *J. Org. Chem.*, **25**, in press (1960).
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