ner was crystallized from methyl alcohol. *Anal.* Calcd. for $C_{35}H_{52}O_4$: C, 78.33; H, 9.77. Found: C, 78.06; H, 9.81. The mixed melting point with an authentic specimen of diacetate from the natural vitamin showed no depression.

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RECEIVED AUGUST 21, 1939

SYNTHETIC APPROACH TO VITAMIN K1

Sir:

In seeking a method for the introduction of the phytyl group into the 3-position of 2-alkyl-1,4-naphthoquinones we have investigated various procedures for condensing 2-methyl-1,4-naphthohydroquinone with phytol, geraniol and simpler β-unsaturated alcohols, and with dienes. In the work on vitamin E such condensations have been brought about in the presence of mineral acids (either added or liberated in the reaction) or zinc chloride and have been attended with cyclization to compounds of the tocopherol type. Since cyclization introduces a complication in the case at hand, trial was made of less powerful agents and it was found that, with anhydrous oxalic acid in dioxane solution, methylnaphthohydroquinone can be condensed with simple β-unsaturated alcohols and dienes to give considerable amounts of the uncyclized substituted hydroquinones. With 2,3-dimethylbutadiene, after refluxing for twenty-four hours, there was obtained 29% of the substituted hydroquinone, characterized as the diacetate (m. p. 119–120°, found: C, 74.04; H, 7.23), and 13% of a stable substance, m. p. 73–73.5°, which appears to be of the tocopherol type (found: C, 79.95; H, 7.63). The crude hydroquinone was converted quantitatively on oxidation to 2-methyl-3-(β,γ,γ-trimethylallyl)-1,4-naphthoquinone, m. p. 95–95.5° (found: C, 80.33; H, 7.25); this gives the above diacetate on treatment with pyridine, acetic anhydride, and zinc dust. Condensation with cinnamyl alcohol gave a hydroquinone (extracted with 10% sodium hydroxide) which formed a diacetate, m. p. 167.5–168° (found: C, 77.17; H, 6.09) and a quinone, m. p. 127–127.5° (found: C, 83.63; H, 5.71).

The reaction is being extended to other examples, including the isoprenoid alcohols, and the use of esters and ethers of the hydroquinone is being investigated. We have ascertained that phytol enters into the condensation under the above conditions or at 140°, and viscous oils have been obtained of the composition of the substituted hydroquinone or tocopherol. One preparation, purified by rather drastic treatment with alkali and by high vacuum distillation, gave C, 82.62; H, 10.52 ($C_{31}H_{48}O_2$ requires C, 82.24; H, 10.69); another after distillation gave C, 82.36; H, 10.71. The general character of the distilled material suggests that it is the tocopherol. In the geranyl series a similar product was oxidized with lead tetraacetate to a substance having the composition of the acetoxyquinone (found: C, 74.92; H, 8.15; $C_{23}H_{28}O_4$ requires C, 74.93; H, 7.69), and this route is under investigation.

Synthesis by the addition of a Grignard reagent to a 2-alkyl-1,4-naphthoquinone oxide does not appear promising. Such oxides (2-methyl, 2,6- and 2,7-dimethyl) are conveniently prepared by adding aqueous sodium carbonate to an alcoholic solution of the quinone and excess hydrogen peroxide. The 2,6-dimethyl compound, m. p. 97–98° (found: C, 71.23; H, 5.07), with either allylmagnesium bromide or magnesium bromide in ether gave a considerable amount of the bromohydrin, m. p. 146–148° (found: C, 51.05; H, 4.18; Br, 28.33), characterized by conversion to the bromodimethylnaphthoquinone, m. p. 114–114.7° (found: C, 54.64; H, 3.61).

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SYNTHESIS OF 2-METHYL-3-PHYTYL-1,4-NAPHTHOQUINONE

Sir:

When equivalent amounts of phytol and 2-methyl-1,4-naphthohydroquinone are heated in dioxane solution in the presence of anhydrous oxalic acid at the reflux temperature, condensation occurs readily but the methylphytylnaphthohydroquinone produced is cyclized about as rapidly as formed and the chief reaction product appears to be the naphthotocopherol. By using a large excess of methylnaphthohydroquinone to accelerate the bimolecular condensation reaction and by operating at a temperature (75°) where cyclization is slow, it is possible to produce a considerable amount of the substituted hydroquinone.