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DIRECT SYNTHESIS OF VITAMIN K_1 AND K_2

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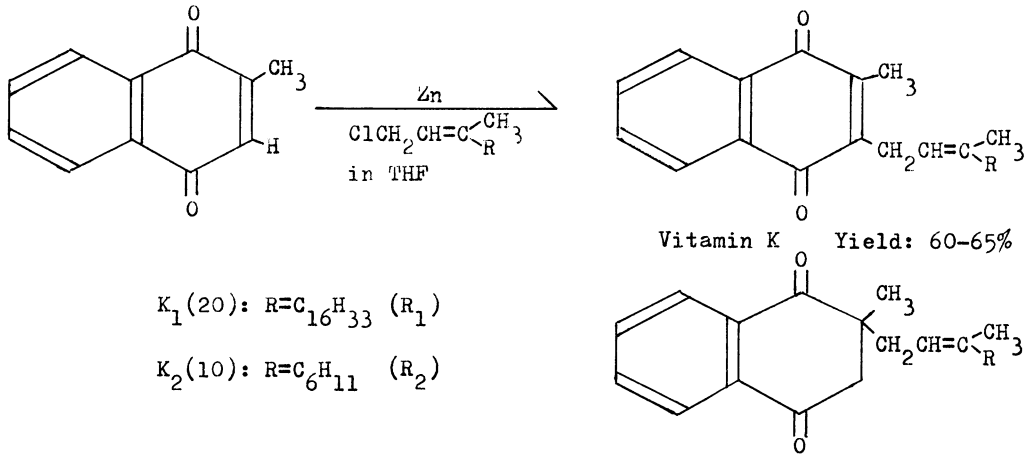
Vitamin K_1(20) and K_2(10) were obtained in good yields by the reactions of 2-methyl-1,4-naphthoquinone with phytyl and geranyl halide in the presence of metal dust. In this method, no reduction oxidation process is involved and the substitution at position 2 to form the isomeric by-product can be blocked effectively.

A series of vitamin K compounds have been synthesized by the reactions of 2-methyl-1,4-naphthohydroquinone with phytyl derivatives in the presence of acid catalysts followed by the oxidation to their quinones.[1,2] However, according to these methods, the isomeric by-product(I) is formed in nearly equal amount to dihydro K. Recently, some attempts have been carried out for the preparation of vitamin K derivatives by employing organometallic complexes.[3,4,5]

The present study was undertaken with the aim of improving the yield and finding a more simple procedure in the synthesis of vitamin K compounds by obviating the competitive formation of (I). It was found that vitamin K_1(20) and K_2(10) were prepared in good yields by the direct reactions of 2-methyl-1,4-naphthoquinone with phytyl and geranyl chloride in the presence of metal dust. The preferential formation of vitamin K compounds can be explained by the reason that the substitution at position 2 to form (I) can be blocked effectively in comparison with the conventional methods described above.



Vitamin K Yield: 60-65%

K_1(20): R=$C_{16}H_{33}$ (R_1)

K_2(10): R=C_6H_{11} (R_2)

(I) Yield: 20-25%

The typical reaction procedure is as follows ; to a tetrahydrofuran solution of 2-methyl-1,4-naphthoquinone (0.1 mol) and zinc dust (0.2 mol) was added dropwise phytyl chloride (0.12 mol) at 50°C. After the mixture was stirred for 8 hr at 50°C, tetrahydrofuran was removed. The residue was extracted with hexane and the extract was washed with aqueous $NaHCO_3$ solution. After drying over anhydrous Na_2SO_4, the extract was condensed under reduced pressure. The crude oil was purified on a silica gel column chromatography to give vitamin K_1(20) (62%) and (I) (R=$C_{16}H_{33}$, 20%).

The reactions proceeded smoothly only when tetrahydrofuran was used as solvent. The reactivity of the metal dust decreased in the order Zn > Pd > Fe > Co > Sn > Cu. The results are summarized in Table 1. The detailed nature of these reactions reported herein needs further clarification and work in progress is aimed at exploring the synthetic utility of this technique.

Table 1 Yields of vitamin K_1 and K_2

Metal dust	R	Yield (%)	$E^{1\%}_{1cm}$ 248 nm(isooctane)
Zn	R_1	62	418
	R_2	65	569
Pd	R_1	45	414
	R_2	41	556
Fe	R_1	36	409
Co	R_1	34	412
Sn	R_1	30	406
	R_2	33	542
Cu	R_1	25	408

solvent: THF, time: 8-12 hr, phytyl or geranyl chloride: 0.12 mol, menadione: 0.1 mol, metal dust: 0.2 mol, temp.: 45-50°C.

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