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Toward higher polyprenols under ‘prebiotic’ conditions

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Abstract—Geraniol and isomers (C_{10}) can be obtained by the condensation of C_5 monoprenols at room temperature in the presence of montmorillonite K-10. It is also possible to obtain farnesol (C_{15}) and isomers by condensation of geraniol with isopentenol. Despite the low yields achieved, these findings support the hypothesis that polyprenyl phosphates may have been formed in prebiotic conditions, and served as constituents of primitive membranes.

Living cells are surrounded by lipidic membranes that universally contain polyprenoids.[1] The difficulty of identifying any reasonable prebiotic mechanism for the formation of *n*-acyl phospholipids had led us to postulate that primitive membranes were constituted of the simplest possible amphiphiles derived from polyprenols, the polyprenyl phosphates, which we have shown to self-organise into vesicles, provided they contain at least 15 carbons in their lipophilic part (two C_{10} chains, or one $C_{\geq 15}$ chain).[2–6] Leaving aside provisionally the vexing problem of the abiotic origin of the C_5 unit, isopentenol or dimethylallyl alcohol, it was easy to formulate in simplistic terms the reaction leading to homologation as an acid-catalysed alkylation of isopentenol **3** by the dimethylallyl cation derived from dimethylallyl alcohol **1**, or from dimethyl vinyl carbinol **2**. We have now shown that it is indeed possible to achieve this homologation and to obtain, from these C_5 units, C_{10} isomers containing geraniol **4**, and from geraniol C_{15} homologues containing farnesol **13**.

Many simulations of prebiotic reactions have involved clays as acidic catalysts, including amino acid formation and amino acid polymerisation, RNA and DNA oligomerisation.[7–11] It has also been suggested that clays were involved in the apparition of the genetic code.[12] This implication of clays in the origin of life was first suggested by Bernal, half a century ago.[13] This choice was justified by the likely presence of clays on primitive earth and by the variety of reactions that they can catalyze.[14] Montmorillonite K10 is the clay most frequently used, both in organic synthesis and in the simulation of prebiotic reactions.[14–17] It has been used in particular in the synthesis of branched polyprenols by Nagano et al.[18]

The reaction conditions were simple: prenol **1** or dimethyl vinyl carbinol **2** and isopentenol **3** (10 equiv.) were stirred for 9 days in the presence of montmorillonite K10 at room temperature. Apolar olefins and ethers were removed by chromatography on silica gel. The mixture of alcohols was benzoylated and analyzed by GC–MS, and the identification of peaks was based on the retention time and the mass spectrum of authentic samples.

Using prenol **1** as a substrate afforded alcohols **4–8** in 57% yield. With dimethyl vinyl carbinol **2**, the yield was 42%. Replacing prenol **1** by **2** did not affect significantly the ratio of the alcohols **4–8** (Table 1). Geraniol **4** represented only 3% of these alcohols; the major products were homoallylic, with a predominance of *trans*-isogeraniol **6**. Such a trend in the regioselectivity

Table 1. Prenylation of isopentenol **3** by **1** or **2** catalyzed by montmorillonite K10[a]

Substrate	Total yield (%)[b,c]	Ratio (%)[c]				
		4	**5**	**6**	**7**	**8**
1	57	3	24	46	12	15
2	42	3	19	52	10	16

[a] 1 ml of **1** or **2** reacted with 10 ml of **3** and 5 g of montmorillonite K10.
[b] Yields are relative to substrates **1** or **2**.
[c] Percentages determined by GC of the corresponding benzoate esters.

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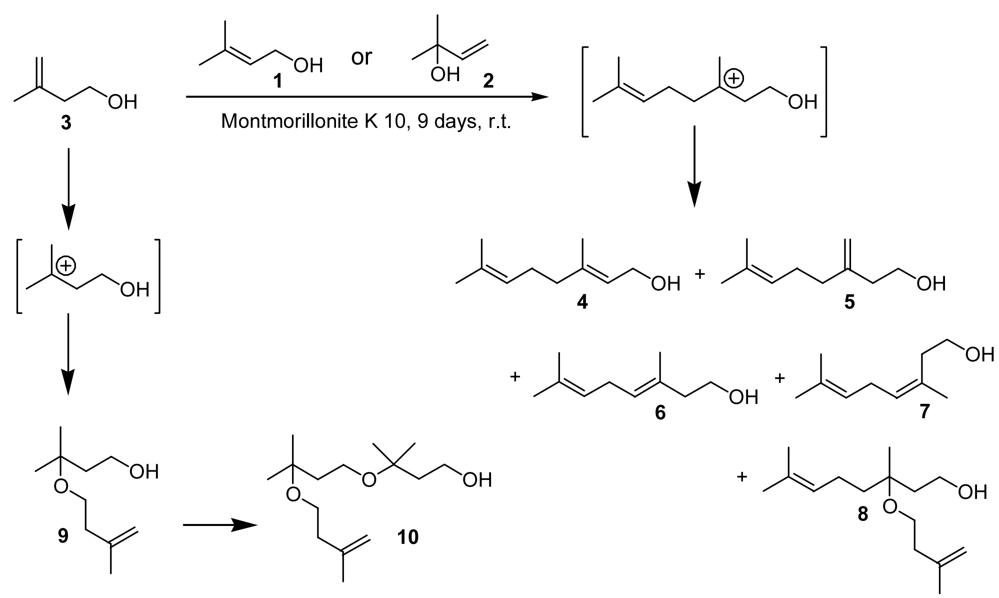
of the proton elimination has been reported by Julia et al. in their studies on biomimetic prenylation reactions.[19] Products **9** and **10** were also formed in 10 and 0.2% yields, respectively, by self-condensation of isopentenol **3** (Scheme 1). Nagai and colleagues have described the same reaction using $BF_3 \cdot Et_2O$, instead of montmorillonite K10, as an acid.[20]

We also checked that geraniol **4** reacts like **1** or **2** to afford C_{15} homoallylic alcohols **11** and **12** as well as a small amount of farnesol **13** in about 15% overall yield (Scheme 2). As previously, the crude mixture was analyzed by GC–MS using authentic benzoyl esters of **11**, *trans*-**12** and **13** as references.

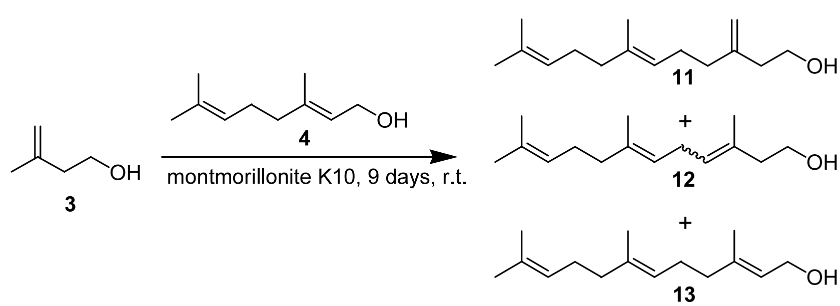
Authentic samples of alcohols **5**, **7** and **9**–**11** were prepared according to described procedures.[20–22]

The synthesis of *trans*-β-isogeraniol **6** and *trans*-β-isofarnesol *trans*-**12** involved Negishi's Zr-catalyzed carboalumination of protected 3-butyn-1-ol with $AlMe_3$ followed by a palladium-catalyzed coupling reaction with prenyl acetate or geranyl acetate (Scheme 3).[23]

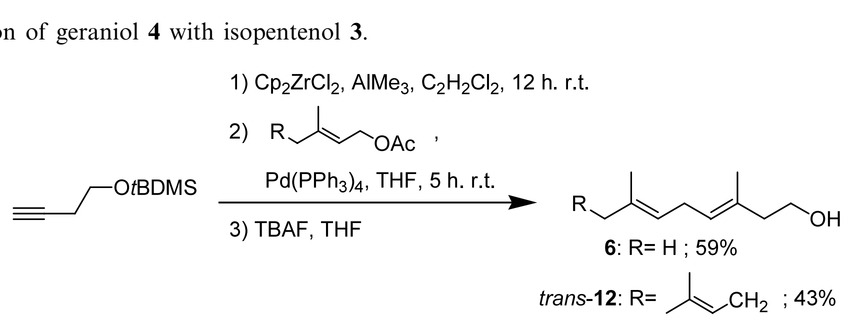
Our data constitute the first evidence that a clay can catalyze an isoprenic condensation. The predominance of homoallylic alcohols **5**–**7** over geraniol **4** may be important in a prebiotic context, because phosphate esters of homoallylic alcohols **5**–**7** would obviously be



Scheme 1. Condensation of **3** with **1** or **2** in the presence of montmorillonite K10.



Scheme 2. Condensation of geraniol **4** with isopentenol **3**.



Scheme 3.

much more stable than the allylic phosphate esters of **4**, and might therefore be candidate primitive phospholipids after further elongation.

The results described, together with the ability of montmorillonite K10 to catalyze phosphorylations,[24] support the hypothesis that clays may have played a role in the genesis of primitive membranes.

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1. Such a bold assertion requires some justification. Archæa contain polyprenyl phospholipids as their membrane matrix; dolichol phosphates are widely present in membranes and are involved in protein glycosylation; geranyl, farnesyl and geranylgeranyl substituents anchor many proteins into membranes; eucaryotic phospholipidic membranes are reinforced by cholesterol and procaryotic ones by hopanoids or α,ω-dihydroxylated carotenoids; ubiquinones ensure electron transfer across membranes; photosynthetic membranes contain phytyl substituted chlorophylls; vision involves retinol, and the photon-driven ion pump of *Halobacterium* retinal.
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