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New Reaction of Aluminum Phenoxide with Terpene Alcohols

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Alkylation is one of the main methods for building the carbon skeleton of a molecule and, therefore, this reaction is of large importance for the organic synthesis of new materials and compounds. Lewis acids, mineral acids, zeolites, and transition metal complexes are known to be used as catalysts in the alkylation of phenols with alcohols. The reaction is carried out in gas and liquid phases under pressure at 80–400°C [1–4]. It is impossible to suggest a single mechanism covering all variations of alkylation reaction because the electrophilic agent can be involved into a polarized complex or react as a carbocation [5–7].

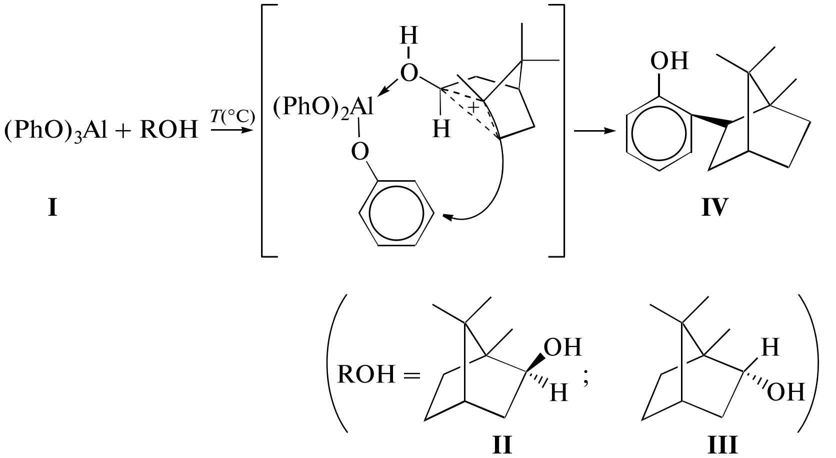
The synthesis of novel terpenophenols with potential physiological activity that behave as highly efficient stabilizers and antioxidants is the actual task of practical importance.

In the present work, we suggest a new reaction of aluminum phenoxide, $(PhO)_3Al$, with terpene alcohols. The reaction proceeds within the coordination sphere of aluminum, and the structure of the alkylating agent plays a leading role [8–11]. The composition of alkylation products was found to be also dependent on reaction temperature.

The structure of alcohol affects the possibility of its hydroxy group to be coordinated to an organoaluminum compound and the subsequent reaction with the aromatic nucleus. Furthermore, the alcohol structure has an effect on the formation of the carbocation whose presence also affects the formation of alkylation products.

The condensation of aluminum phenoxide (**I**) with isoborneol (**II**) results mainly in C-alkylated phenol (**IV**) with a terpene substituent of isobornyl structure in the *ortho* position to the OH group (58%) at 160°C and short reaction time (2 h), indicating the high reactivity of the *exo* hydroxy group (Scheme 1).The reaction of aluminum phenoxide with borneol (**III**), a stereoisomer of isoborneol, requires heating of the reaction mixture up to 170–180°C for 7 h; the yield of *o*-isobornylphenol (**IV**) was 48% (Scheme 1).

The reaction of alcohols with phenoxide $(PhO)_3Al$ or a mixture of phenol with aluminum isopropoxide $(i\text{-}PrO)_3Al$ is supposed to occur within the aluminum coordination sphere. Each of these aluminum compounds has a different effect on the reaction of phenol with terpene alcohols and, hence, on the composition



Scheme 1.

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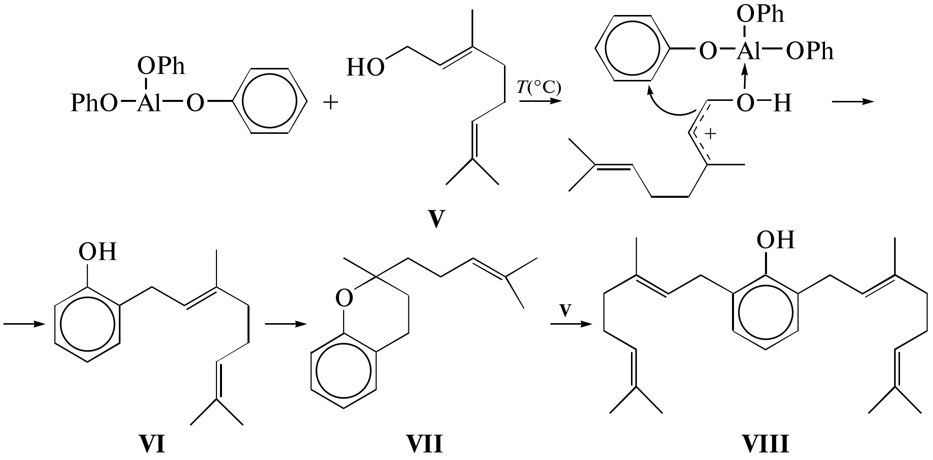


Scheme 2.

of alkylation products. According to the literature data, aluminum phenoxide is strongly associated and exists as dimer even at high temperatures [12, 13]. The hydroxy group of an alcohol (for example, geraniol) is coordinated to the aluminum atom, a partial positive charge appears at the alcohol carbon atom that interacts with the nucleophilic nucleus of the phenoxy group. A supposed reaction route is depicted in Scheme 2.

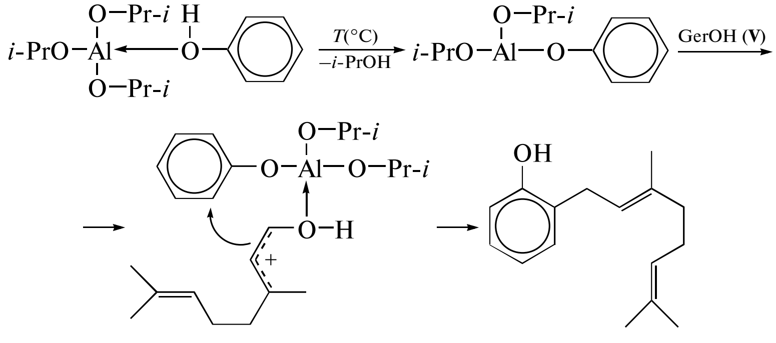
The reaction of aluminum phenoxide with geraniol (**V**, GerOH) at 80°C proceeds unexpectedly with high regioselectivity without allyl isomerization to give *o*-geranylphenol (**VI**, 41%), which converts at 120°C into a chroman-type ether (**VII**, 58%). Increasing temperature of the reaction mixture to 140°C leads to formation of 2,6-digeranylphenol (**VIII**, 57%) (table).

The alkylation of phenol in the presence of $(i\text{-PrO})_3Al$ is accompanied by the formation of mixed aluminum phenoxide–alkoxide (Scheme 3). Since phenol is a stronger acid than alcohol, it displaces the isopropoxy group at the aluminum atom in the aluminum isopropoxide molecule, and then the reaction proceeds through the formation of coordination bond. The formation of aluminum phenoxide from $(i\text{-PrO})_3Al$ at 80°C occurs slowly: the phenoxy group poorly displaces the isopropyl groups at the aluminum atom in the aluminum isopropoxide molecule. When temperature increased, the reaction proceeds selectively through the formation of *o*-geranylphenol (**VI**). It should be noted that the alkylation of phenol with geraniol with the use of $(i\text{-PrO})_3Al$ results in the products of C-alkylation (up to 80%, table). Small

Reaction conditions and products of alkylation reaction of aluminum phenoxides with geraniol

Reagents (ratio)	Reaction conditions	Reaction product, %				
		VI	**VII**	**VIII**	**IX**	PP*
$(PhO)_3Al$/GerOH (1 : 1)	140°C, 4 h	–		57	6	22
	120°C, 4 h	–	58	25	–	16
	80°C, 3 h, benzene	41	17	–	12	24
$(i\text{-PrO})_3Al$ + PhOH/GerOH (1 : 1 : 1)	140°C, 4 h	10	–	63	6	20
	120°C, 4 h	67	2	2	5	15
	80°C, 3 h, benzene	No reaction				

* Inseparable mixture of polymerization products (PP).



VI

Scheme 3.

amounts of 4-geranylphenol (**IX**) were isolated from a mixture of reaction products.

Thus, we have shown in this work the high reactivity of aluminum phenoxide toward activated terpene alcohols.

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