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A Quantum Mechanical Study on Carbocation Formation Energy in (Poly)Ethylenic Compounds.

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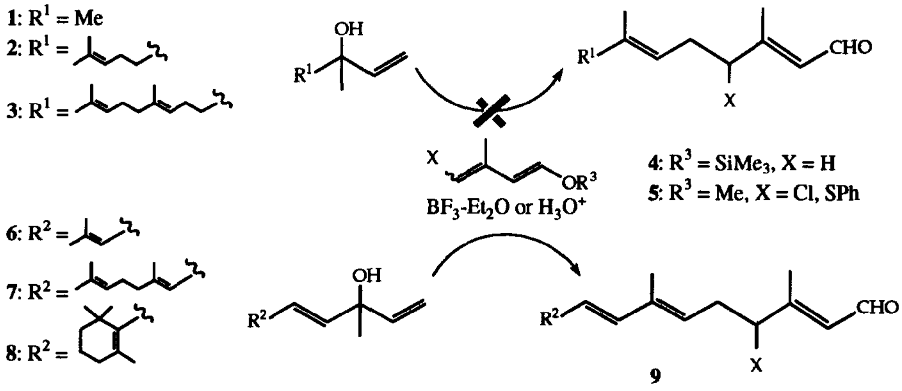
Abstract: Semiempirical and *ab initio* calculations on (di)allylic alcohols indicate that the efficiency of their acid-catalyzed condensation with dienol ethers depends on their protonation-dehydration energies.

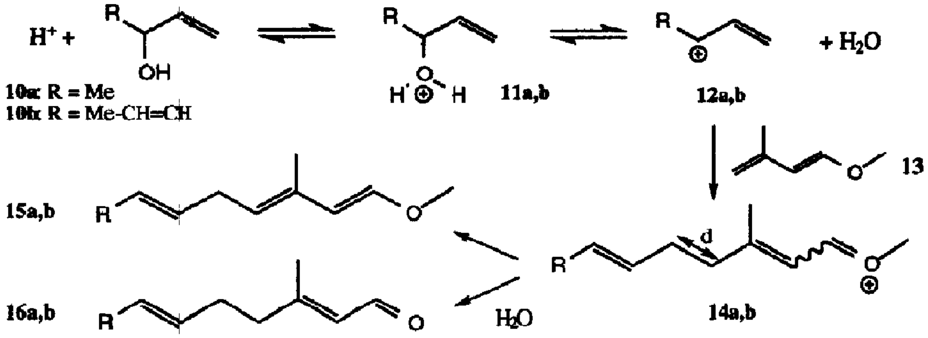
The polyethylenic compounds constitute a class of molecules constantly in the forefront of experimental[1] and theoretical[2] chemical research mainly because of their biological significance[3], their major implication in molecular electronics[4] and the long-lasting synthetic challenge they represent. Among the new accesses proposed for these compounds, three of us have recently been interested in the carbocationic coupling between (poly)ethylenic alcohols (**1-3**, **6-8**) and various enol ethers (**4**, **5**) in a protic aqueous medium or in organic solution in presence of Lewis acids[5]. These results, obtained in remarkably mild conditions (-10°C, aqueous formic acid), have pointed out the existence, in the alcoholic moiety, of structural factors of critical importance. For instance, while unsaturated alcohols (such as 3-methyl-but-1-en-3-ol **1**, linalol **2** or nerolidol **3**) remained to a great extend unaltered when opposed to enol ethers **4** or **5** in presence of BF_3-Et_2O or in aqueous formic acid, the corresponding alcohols featuring both β,γ and β',γ' unsaturations (such as linalol **6**, vinyl-ψ-ionol **7** or vinyl-β-ionol **8**) turned out to provide the expected terminaly functionalized coupling aldehydes **9** in good to high yields (Scheme 1).



Scheme 1.

A likely mechanism for this type of reaction goes through the protonation or the complexation by the Lewis acid of the hydroxy group, leading to a carbocation on which the condensation of the enol ether takes place (Scheme 2).[5,6] The occurence of a regioselective addition at the terminal position of these cations rises the question of the exact nature of the factors contributing to the generation/stabilization of such species.

We have therefore undertaken a set of theoretical calculations in order to compare simple models of the two series of above alcohols (**10a,b**), their protonated form (**11a,b**), the corresponding dehydrated cations (**12a,b**) and intermediate oxoniums (**14a,b**) derived from the addition of a simple enol ether, closely related to those experimentally studied, on these cations (Table 1). This investigation has furthermore been limited to the protic acid conditions since the experimental works using BF_3-Et_2O have led to the same products in comparable yields[5]. These computations have been performed at two different levels of theory. An exploratory study using AM1[7] was first undertaken in order to determine the factors possibly responsible for the observed difference of reactivity between the alcohols bearing only one double bond versus the polyethylenic ones. We have then checked the consistency of these results at a more refined level of computation, performing an *ab initio* SCF study using the 6-31G** basis set followed by a second order Møller-Plesset (MP2) perturbation treatment of the correlation energy[8].



Scheme 2.

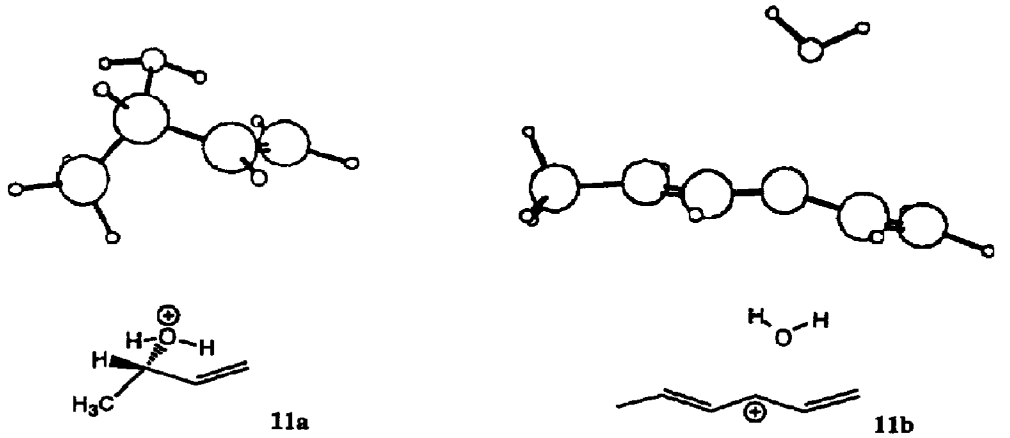
The AM1 complete optimization, using gradients technic, of the structures involved in the expected reactional pathway (Scheme 2) has led to the energy differences reported in Table 1. We have repeated these calculations with the more elaborated MP2/6-31G** procedure for the key-compounds **10**, **11** and **12**. The AM1 results for the alcoholic substrates **10**, their protonated forms **11** and the corresponding carbocations **12** show that the protonation and dehydration of the alcohols is more favorable for R = Me-CH=CH than for R = Me (18.5 and 14.0 kcal/mol, respectively). More important are the differences found between the AM1 theoretical structures for the two protonated alcohols. For R = Me (**11a**), the calculated C-OH_2 bond length is $l = 1.65$ Å, the OH_2 group carries a net charge of +0.397e and the carbocation part is definitely not planar. By contrast we obtain, for R = Me-CH=CH (**11b**), a structure best described as a complex between a carbocation and a water molecule as demonstrated by $l = 3.17$ Å, the negligible net charge of the water moiety (+0.005 e) and the planarity of the carbocationic part with a geometry close to that obtained for the isolated entity **12b** (Fig. 1). On the other hand, results dealing with the condensation between the carbocations **12** and enol ether **13** yielding to oxoniums **14** indicate this reaction to be easier in the R = Me case by 11.5 kcal/mol. In absence of water, the passage to enol ethers (**14** → **15**) would no longer depend on oxoniums structure ($\delta\Delta E = 0.0$).

Table 1. AM1 and *Ab Initio* Energy Variations (in kcal/mol) Calculated for the Different Steps of the Postulated Mechanism (Scheme 2).

Step	AM1			MP2/6-31G**		
	a: R = Me	b: R = Me-CH=CH	δΔ(E)	a: R = Me	b: R = Me-CH=CH	δΔ(E)
10 → 11	-131.4	-149.9	-18.5	-195.3	-216.3	-21.0
11 → 12	4.6	9.2	+4.6	11.4	10.5	-0.9
10 → 12	-126.8	-140.7	-14.0	-183.9	-205.8	-21.9
12 → 14	-53.0	-41.5	+11.5	[a]	[a]	-
14 → 15	161.4	161.4	0.0	[a]	[a]	-

[a] not performed at this level of theory.

The MP2/6-31G** values in Table 1 show an excellent overall agreement with the AM1 results. The comparison for the protonated alcohols **11a,b** of *ab initio* values for the relevant geometrical parameters (l = 1.61 and 2.80 Å, respectively) and charge distribution (+0.374 and +0.015e on OH_2, respectively) with the AM1 ones allows to draw identical conclusions (Fig. 1). The ≈ 20kcal/mol preference in favor of **11b** with respect to **11a** may be ascribed to the stabilization produced by the formation of a planar conjugated system. In addition, the [δΔ(E)] accounting for the relative stabilization[9] of **12b** is emphasized at the non-empirical level. The crucial importance of the initial steps of this reaction (leading to carbocations **12**) is thus confirmed by this more elaborated second set of results. Last but not least, the AM1 results also indicate that no activation energy is necessary for the **12** → **14** condensation reaction (Figure 2), putting further emphasis on the importance of this protonation-dehydration step.



11a

11b

Figure 1. MP2/6-31G** optimized structures of the protonated alcohols **11a** and **11b**.

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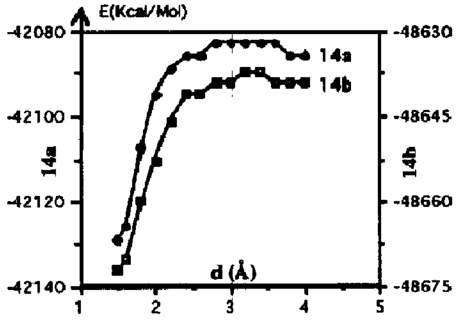

Figure 2. AM1 energy variation (in kcal/mol) of **14a,b** as a function of the length of the bond (d, *Scheme 2*) created during the condensation.

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