

# A note on the role of methanol in the homogeneous and heterogeneous acid-catalyzed hydroxymethylation of guaiacol with aqueous solutions of formaldehyde

F. Cavani\*, M. Corrado, R. Mezzogori

*Dipartimento di Chimica Industriale e dei Materiali, Viale Risorgimento 4, 40136 Bologna, Italy*

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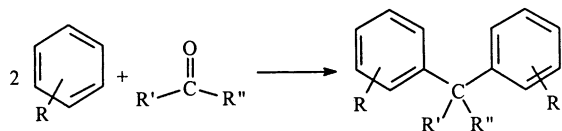
## Abstract

The acid-catalyzed hydroxymethylation of 2-methoxyphenol (guaiacol) with formaldehyde aimed at the synthesis of benzyl alcohol derivatives (vanillic alcohols) was studied with specific attention being given to the role of methanol which is present in commercial aqueous solutions of formaldehyde. Methanol had a pronounced effect on the catalytic performance with both homogeneous and heterogeneous acid catalysts. Specifically, the conversion of guaiacol decreased considerably with increasing amounts of methanol in the formaldehyde solution, and the distribution of products is also changed. In the absence of methanol the formation of diaryl compounds predominated over the formation of monoaryl by-products. © 2002 Elsevier Science B.V. All rights reserved.

*Keywords:* Hydroxymethylation; Guaiacol; Formaldehyde; Vanillic alcohols

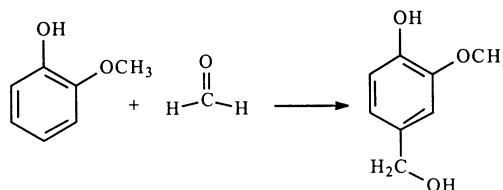
## 1. Introduction

A reaction of interest for the production of intermediates and specialty chemicals is the condensation of carbonyl compounds with arenes, aimed at the production of diarylmethanes [1], for instance, bisphenol A preparation is based on this reaction. An analogous



reaction is the hydroxyalkylation of activated arenes (thus containing functional groups such as hydroxy or methoxy groups) [2–4] and furan derivatives [5,6]

with aldehydes and ketones; in this case, the reaction is aimed at the introduction of one hydroxyalkyl group on the aromatic ring, yielding intermediates for the production of drugs, polymers and food additives. This reaction represents one-step in a multi-step synthesis of 3-methoxy-4-hydroxybenzaldehyde (vanillin), an environmentally friendly process for the production of this important food additive [10,11].



At the industrial level, this class of reactions is catalyzed by Lewis-type acids, such as  $\text{AlCl}_3$ , and by mineral Brönsted acids, as well as by bases. Some

\* Corresponding author.

*E-mail address:* cavani@ms.fci.unibo.it (F. Cavani).

papers have appeared in recent years, where zeolitic materials are described as catalysts for this reaction [1–6]. Solid acid materials are highly desirable catalysts, since the environmental impact of the process benefits from easier separation of the catalyst from the products mixture, the absence of liquid wastes containing inorganic salts, and fewer corrosion problems.

Usually, the hydroxymethylation is carried out in the liquid phase, and large pore zeolites are necessary in order to make the reaction occur at an acceptable rate in the condensed phase. One main problem is the presence of water, since the aqueous solution of formaldehyde (formalin) is the simplest, cheapest and largely available reactant to be employed from the commercial point of view. This implies the need for hydrophobic zeolites, in order to avoid that the pores become filled preferentially by more polar molecules rather than by the aromatic substrate [7,8]. For this reason, mordenites and  $\beta$ -zeolites are considered to be the optimal ones for the reaction; the hydrophobicity of these materials can be tuned by the Si/Al ratio [7–9].

Another aspect, which has not yet been analyzed in the literature, is the possible effect of methanol—which is added in commercial formalin solutions to inhibit formaldehyde polymerization—on catalytic performance. Aim of the present work was to analyze the effect of this parameter, under both homogeneous and heterogeneous acid-catalyzed conditions, in the reaction of hydroxymethylation of 2-methoxyphenol (guaiacol) with formalin.

## 2. Experimental

Catalytic tests were carried out in a glass, batch reactor, loading 48 ml of commercial aqueous solution of formaldehyde, and either 1 g of solid catalyst (for tests carried out under heterogeneous conditions), or 0.15 ml of Conc.  $H_2SO_4$  for homogeneous tests. The mixture was then heated at 80 °C, and 4 ml of guaiacol were added under stirring. The reaction mixture was left at 80 °C under vigorous stirring (600 rpm).

In the commercial aqueous solution of formaldehyde (typically containing 37 wt.% formaldehyde and 10–15% methanol), the monomeric form of formaldehyde (around 40% with respect to total formaldehyde) is mostly present in the form of methylene glycol with a small amount of hemiformal and around 0.1%

of formaldehyde as such, while the remaining 60% of formaldehyde is in the oligomeric form (polyoxymethylene glycols and polyoxymethylene hemiacetals) with a distribution of molecular weights which is a function of the methanol content in the solution. Methanol inhibits the formation of higher molecular weight polyoxymethylenes, which would precipitate and separate from the aqueous solution.

In tests carried out using non-commercial aqueous solutions of formaldehyde, with a methanol content between 0.5 and 15%, the reactant solutions were prepared by adding controlled amounts of methanol to an aqueous solution containing 29–30 wt.% formaldehyde and 0.5–1.5 wt.% of methanol. In this case, the formaldehyde concentration in water was lower than that usually found in commercial solutions, since otherwise the solution would be unstable. In these reactivity tests, the polyaryl compounds were insoluble in the aqueous phase, and formed a separate oil phase; therefore, they were indirectly determined as lack in the C balance.

The products were analyzed by HPLC (TSP Spectra Series), equipped with a Alltech Hypersil ODS column, and with UV–Vis TSP UV150 detector ( $\lambda$ , 280 nm). Elution was done with a mixture of acetonitrile and water. Identification of products was made by GC–MS and by comparison with the retention time of standard components (when available). For heterogeneous tests a commercial zeolite has been used, a H-mordenite HM-45 supplied by Engelhard characterized by a Si-to-Al atomic ratio equal to 23.

## 3. Results and discussion

### 3.1. Heterogeneous catalysis: reactivity with H-mordenite catalyst

From the various zeolitic catalysts claimed to give optimal catalytic performance [12], we chose a commercial mordenite to carry out the catalytic tests of guaiacol hydromethylation and to check the effect of methanol in the reaction medium. The following products were identified (Fig. 1):

1. Vanillic alcohols (VAs): *o*-VA: 2-hydroxy-3-methoxybenzyl alcohol, or isovanillool; *m*-VA:

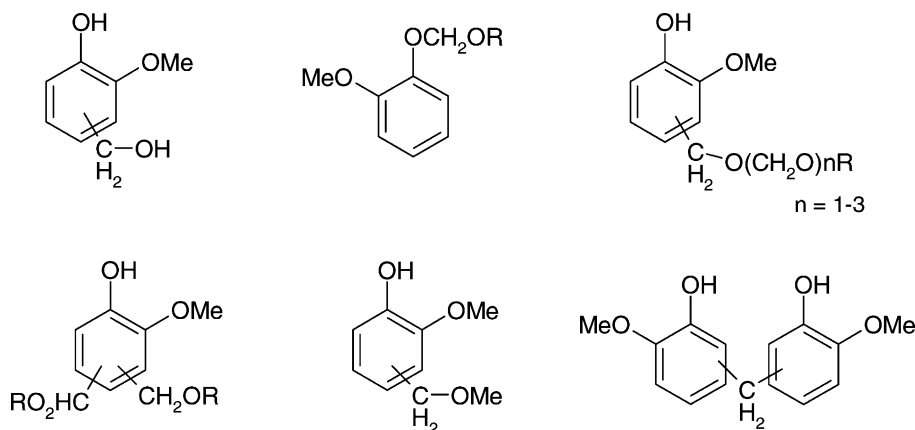


Fig. 1. Main products obtained in the hydroxymethylation of guaiacol with formaldehyde. R = -H or -CH<sub>3</sub>.

3-hydroxy-4-methoxybenzyl alcohol and 3-hydroxy-2-methoxybenzyl alcohol (the formation of the latter isomer, however, was negligible); *p*-VA: 3-methoxy-4-hydroxybenzyl alcohol.

2. Monoaryl products other than vanillols, mainly constituted of: (a) the product of *O*-hydroxymethylation; (b) the products of hydroxyalkylation by hemiformal or polyoxymethylene glycols or polyoxymethylene hemiacetal; (c) the products of di-hydroxyalkylation; (d) the products of etherification of vanillols by methanol; (e) the products of C-alkylation by methanol (which, however, were present in traces).
3. Diaryl compounds of MW 260, which corresponds to the bisarylmethane obtained by condensation of one molecule of vanillic alcohol with guaiacol, and of MW 290, obtained by condensation of two molecules of vanillic alcohols, as schematized in Fig. 2. Traces of triaryl compounds (MW 396) were also found. The formation of high-molecular-weight phenolic resins was not observed under our reaction conditions, except for a few specific cases.

Results of catalytic tests carried out by changing the initial methanol-to-formaldehyde molar ratio in the batch are plotted in Fig. 3 (top: conversion of guaiacol and distribution of the products; bottom: selectivity to the three VA isomers). The effect of methanol on catalytic performance was remarkable: (i) the conversion of guaiacol progressively decreased

and (ii) the distribution of the products changed with increasing methanol-to-formaldehyde ratio. Specifically, while in the substantial absence of methanol the prevailing by-products were diaryl compounds, with increasing methanol content formation of the latter decreased and formation of monoaryl compounds other than vanillols increased.

The main contribution for the effect of methanol on guaiacol conversion is likely a kinetic one; since the prevailing by-products in the presence of low methanol concentrations were diaryl compounds, this implies a higher conversion of the aromatic reactant owing simply to stoichiometric reasons. Also, a contribution might come from a change in the partition factor of formaldehyde between the gas phase and the liquid phase, which is influenced by methanol concentration [13].

Another factor which may contribute in affecting the conversion of guaiacol is the competition between methanol and formaldehyde on the active sites. Since the nucleophilicity of the O atom decreases in the order: water > methanol > formaldehyde > guaiacol (for the protonation of the hydroxy group), as inferred from the corresponding  $pK_a$  values (H<sub>2</sub>O, -1.7; CH<sub>3</sub>OH, -2.2; H<sub>2</sub>CO, -4; phenol, -6.7), this implies that in aqueous medium the formation of hydroxonium H<sub>3</sub>O<sup>+</sup> by water protonation is largely preferred (and this species becomes the active one) [14], and that methanol has a higher affinity for protons than formaldehyde, and thus competes with the latter.

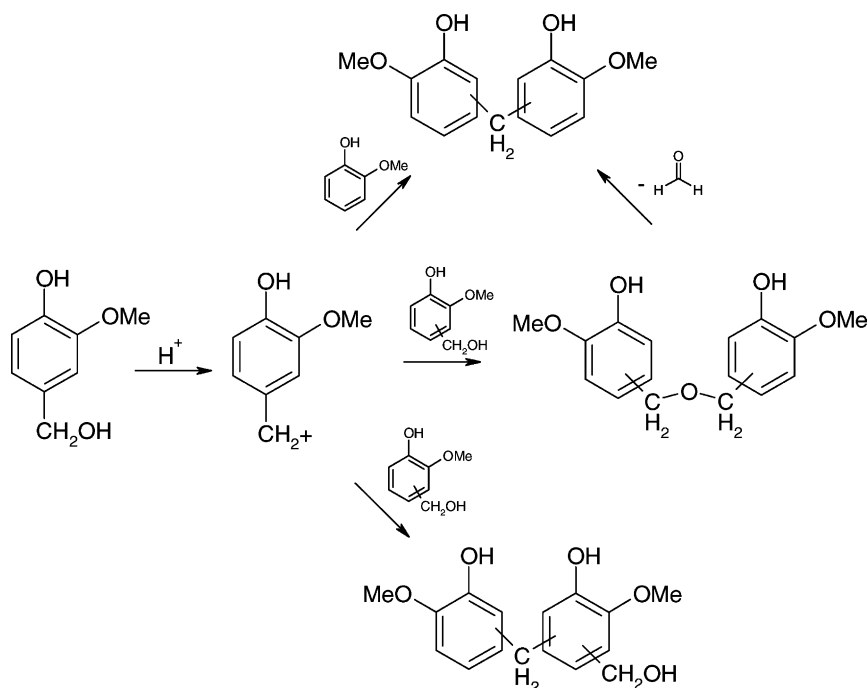


Fig. 2. Consecutive reactions leading to the transformation of VAs to diaryl by-products.

The effect of methanol concentration on the selectivity is a consequence of the different levels of conversion which were achieved, but might also be due to a chemical effect. Thus, the alcohol might play the same role as it does in formalin solution, with formation of monoaryl compounds (e.g., ethers), and inhibition of the consecutive transformation of VAs to diaryl compounds. Indeed, it is known that in the industrial production of resins, methanol can intervene in the polycondensation reaction by the formation of ethers, acetals and hemiacetals, and for this reason methanol concentration should be as low as possible.

In order to distinguish between the different possible contributions, tests were done with varying reaction time and using a formaldehyde solution containing 0.5 wt.% of methanol. The results are reported in Fig. 4. The conversion of guaiacol increased with increasing the reaction time. The formation of by-products was relevant (selectivity around 30%) even at low guaiacol conversion, and in this case prevailing by-products were monoaryl and diaryl

compounds. With increasing conversion, the selectivity to the by-products increased, due to the substantial contribution of the consecutive condensation of VAs into diaryl compounds, occurring mainly at the expense of *p*-VA. After 3 h reaction time, the only products obtained were heavy, polyaryl compounds.

The effect of reaction time on catalytic performance in the presence of methanol is shown in Fig. 5. In this case, a contribution to consecutive reactions also came from the reactions of VAs with methanol and with hemiformal yielding monoaryl by-products.

In all cases, the main consecutive reactions were on *p*-VA, as clearly shown in Figs. 3–5. This occurs because in the  $\text{O-CH}_2^+$  species which develops by protonation of the hydroxymethyl group and exit of water, the positive charge is delocalized in the aromatic ring in those positions where the mesomeric effect of the hydroxy group is more effective. In *o*-VA, the combination of mesomeric and inductive effects makes the corresponding cation less stabilized; moreover, a shape-selectivity effect might inhibit the transformation of this molecule (which is sterically

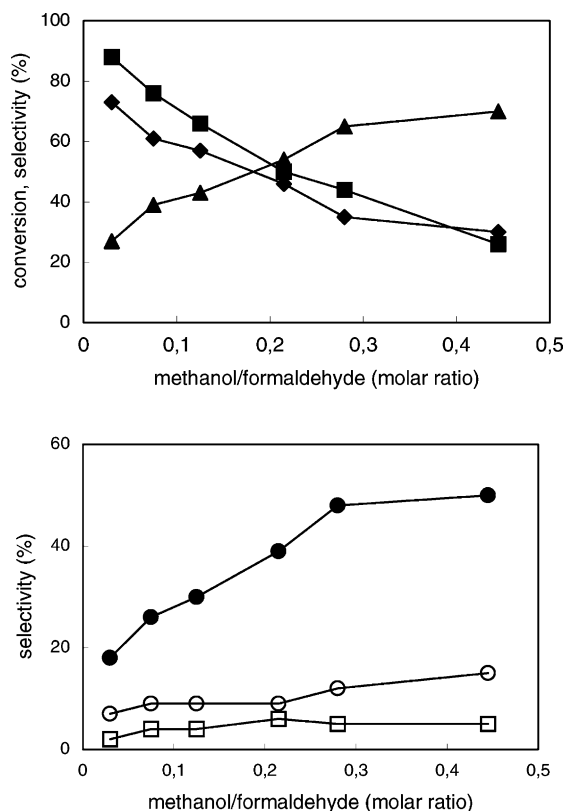


Fig. 3. Effect of the methanol-to-formaldehyde molar ratio on (top): guaiacol conversion (■), selectivity to vanillols (▲) and selectivity to by-products (◆); (bottom): selectivity to *p*-VA (●), *o*-VA (○) and *m*-VA (□). Reaction time, 120 min; temperature, 80 °C. Starting with formalin (aqueous solution containing 29 wt.% formaldehyde and 1.5 wt.% methanol), to which increasing amounts of methanol were added. Initial formaldehyde/guaiacol molar ratio is 14.

more hindered than *p*-VA), and the nucleophilicity of the O atom in the hydroxymethyl group is lower due to the fact that an intramolecular H-bridging between the two adjacent substituents may occur.

Fig. 6 compares the selectivity of the products as functions of the conversion for data plotted in Figs. 4 and 5. It is shown that the selectivity to VAs was systematically higher for tests carried out in the presence of methanol; this difference, therefore, arises from the lower extent of parallel reactions which occur in the presence of methanol, likely due to the different nature of by-products which are formed in the two cases.

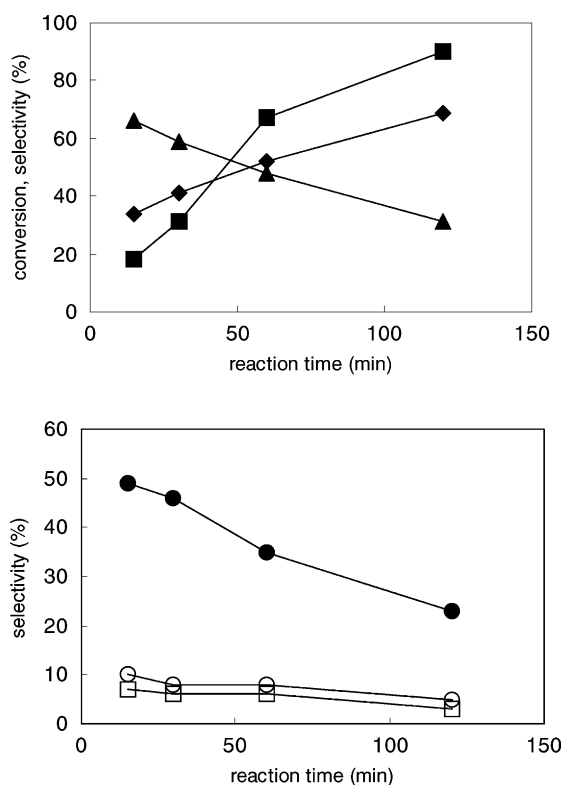


Fig. 4. Effect of the reaction time on catalytic performance. Symbols as in Fig. 3. Temperature is 80 °C. Formalin: aqueous solution containing 30 wt.% formaldehyde and 0.5 wt.% methanol. Initial formaldehyde/guaiacol molar ratio is 14.

### 3.2. Homogeneous catalysis: reactivity with sulfuric acid

Tests have been done with a homogeneous acid ( $\text{H}_2\text{SO}_4$ ), to check whether the observed effects were also detected under such conditions. The results are summarized in Table 1, which reports the conversion of guaiacol, and the selectivity to the different classes of products, as functions of the reaction time, for tests carried out with the commercial solution of formaldehyde. For short reaction times, the prevailing by-products were monoaryl compounds other than vanillols; amongst the latter, the prevailing compound was *p*-VA. This distribution of VAs comes from a balance of the mesomeric (stronger for the hydroxy than for the methoxy group) and inductive effects of the two substituents. This also points out the considerable

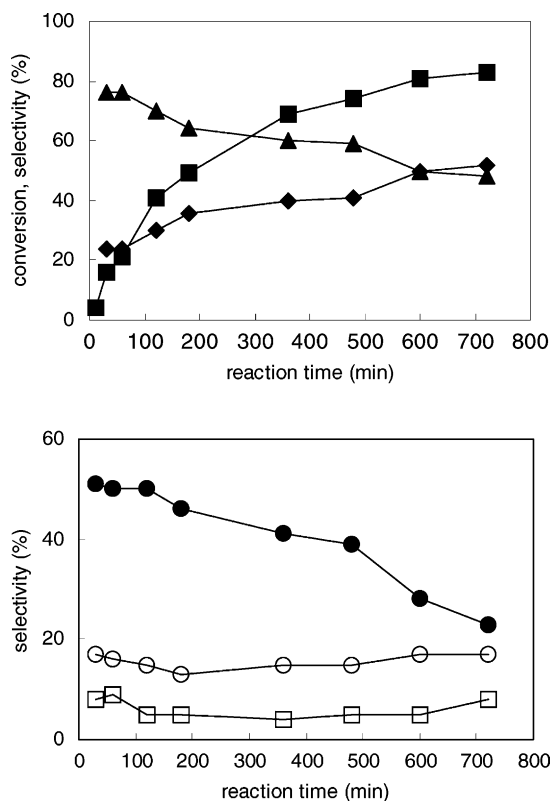


Fig. 5. Effect of the reaction time on catalytic performance. Symbols as in Fig. 3. Temperature is 80 °C. Formalin: aqueous solution containing 37 wt.% formaldehyde and  $\approx$ 10–15 wt.% methanol. Initial formaldehyde/guaiacol molar ratio is 18.

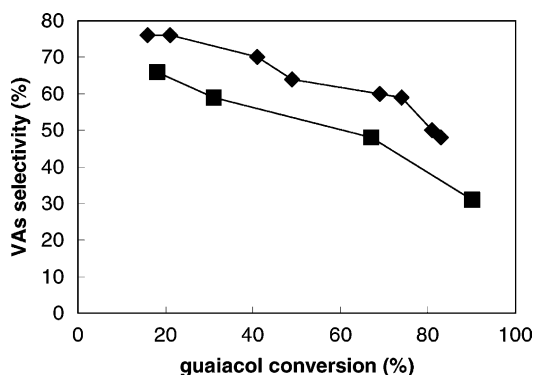


Fig. 6. Selectivity to VAs as a function of the guaiacol conversion for tests carried out with the aqueous solution containing 30 wt.% formaldehyde and 0.5 wt.% methanol (■), and with aqueous solution containing 37 wt.% formaldehyde and  $\approx$ 10–15 wt.% methanol (◆).

Table 1

Guaiacol conversion and distribution of the products as functions of the reaction time with H<sub>2</sub>SO<sub>4</sub> catalyst<sup>a</sup>

Reaction time	Guaiacol conversion (%)	Selectivity (%)			By-products (%)
		<i>o</i> -VA	<i>m</i> -VA	<i>p</i> -VA	
30	26	12	10	22	56
85	35	12	5	11	72
140	58	5	3	5	87
85 <sup>b</sup>	72	4	2	4	90

<sup>a</sup> Catalyst volume, 0.15 ml; formaldehyde aqueous solution containing 37 wt.% formaldehyde and  $\approx$ 10–15% methanol. Temperature is 80 °C, formaldehyde/guaiacol molar ratio is 18.

<sup>b</sup> Formaldehyde aqueous solution containing 29 wt.% formaldehyde and 1.5% methanol. Reaction time is 85 min.

shape-selectivity effect observed with the mordenite catalyst (Figs. 3–5), which further enhances the formation of the *p*-isomer with respect to the *o*-isomer.

After 85 min reaction time, *p*-VA and *o*-VA were obtained in comparable amounts, and both were approximately twice that of *m*-VA; this ratio then remained approximately constant for longer reaction times, while the overall selectivity to VAs decreased with increasing the guaiacol conversion. It is likely that the distribution of the isomers obtained after 85 min corresponds to the thermodynamic distribution, and that therefore under these reaction conditions and with sulfuric acid the thermodynamic equilibrium for the reaction of isomerization is reached.

Data clearly indicate that, analogously to that observed with the H-mordenite, the monoaryl by-products are formed via parallel reactions, since the corresponding selectivity is high even at relatively low guaiacol conversion. Also in this case, as for heterogeneous tests, the main by-products were monoaryl compounds. For increasing values of guaiacol conversion, the selectivity to monoaryl and diaryl compounds increased, with a corresponding decrease in selectivity to VAs.

A test was made by using a formaldehyde aqueous solution containing 1.5 wt.% methanol (Table 1). Under these conditions, the conversion of guaiacol was higher, and diaryl compounds were the prevailing products, obtained by consecutive reactions upon VAs. The effect was thus very similar to that observed with the H-mordenite.

#### 4. Conclusions

Catalytic tests of guaiacol hydroxymethylation have been performed in both homogeneous and heterogeneous acid reaction media. The phenomenology was similar in the two cases; the reaction network consists of parallel reactions of the formation of vanillic alcohols and of monoaryl by-products, while consecutive reactions mainly involve the transformation of VAs (especially *p*-VA) to monoaryl and diaryl by-products. An important effect was due to the presence of methanol (contained in the formalin solution) in the reaction medium; methanol decreased guaiacol conversion and changed the distribution of the products with respect to the case when the reaction was carried out with minimal methanol concentration. In the latter case, diaryl by-products formed preferentially at both low and high conversion.

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