

Review

## Acid Catalyzed Reactions of Substituted Salicylaldehydes with 2-Methylfuran

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**Abstract:** Data, concerning condensation reactions of salicylaldehydes and 2-methylfuran are generalized. During the course of investigation a sequence of proceeding transformations is established. It is shown that it is possible to obtain 2-hydroxyarylbis(5-methylfur-2-yl)methane, benzofuran or oxazulene derivatives selectively by simple changing of the reaction conditions.

**Keywords:** substituted salicylaldehydes, 2-methylfuran, 2-hydroxyaryldifurylmethanes, benzofuran, disproportion, oxazulene derivatives.

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### Introduction

Difurylalkanes have a wide spectrum of practical use as monomers [1-3], modifiers [4,5], cross-coupling reagents [6,7] allowing to lower cost [8,9] and to expand assortment of polymer materials [10] in plastic manufacture. Some compounds of this class are of interest in dye chemistry [11] and copy engineering [12], in synthesis of macrocyclic compounds which are used as metal ions carriers [13, 14]. The difurylalkanes are of interest for food industry since they were found among numerous

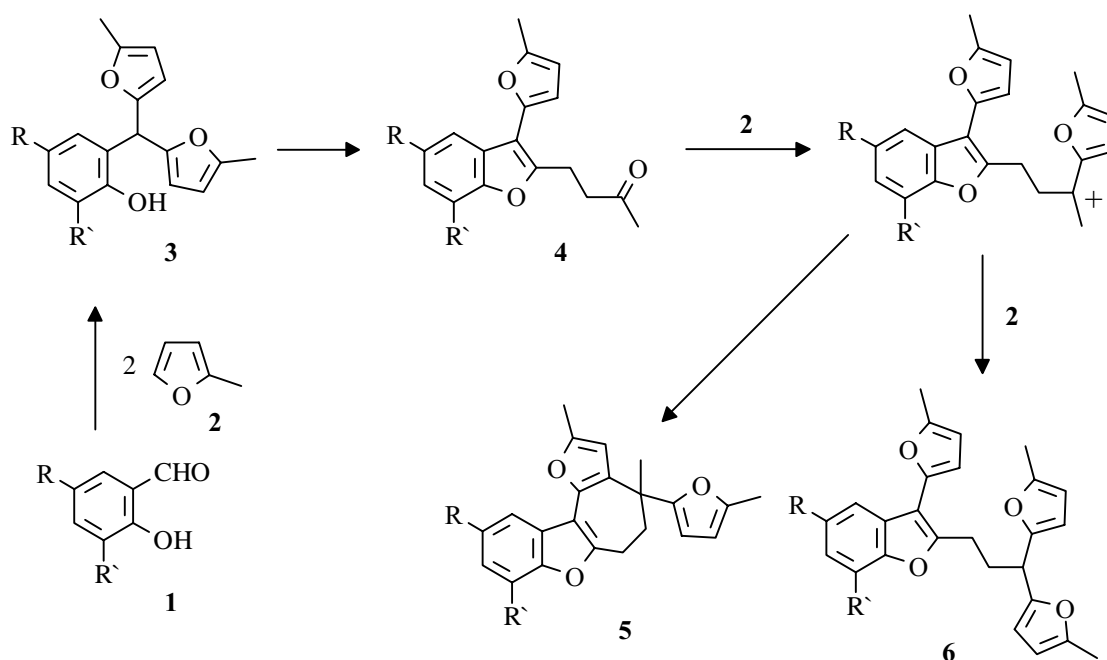
compounds making up coffee aroma [15] and other products [6-18]. Difurylmethane fragment is a component of structure of a number of fungicides [19].

Unfortunately, up to date these compounds have found a little application as synthones in organic synthesis. Structure of difurylalkanes and furan ability to serve as convenient 1,4-diketone equivalent in many chemical reactions [20, 21] provide easy access to different classes of carbo- and heterocyclic compounds. Earlier it was reported about the synthesis of carbazole [22, 23], cyclopentenone [24], cynnoline and benzothiazine [25], indole and azaazulenium derivatives [25-27] starting from difurylmethanes.

In this work we wish to present our data on the reaction of substituted salicylaldehydes and 2-methylfuran which proceeds with initial formation of 2-hydroxyaryldifurylmethanes and their subsequent transformation into benzofuran and oxazulenium derivatives.

## Discussion

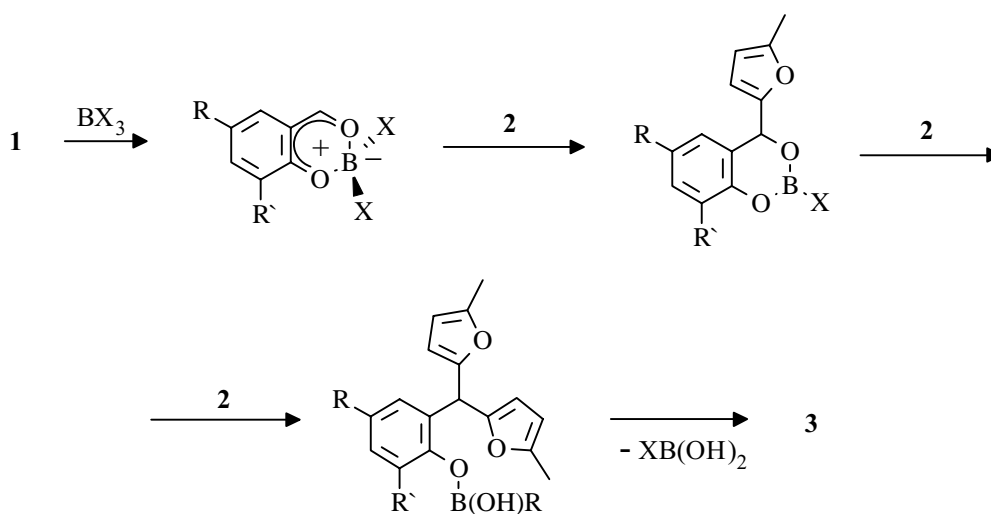
Preliminary results of salicylaldehydes **1** interaction with 2-methylfuran **2** in the presence of  $Mg(ClO_4)_2$  and  $HClO_4$  [28, 29] had shown that along with the basic products of reaction - 2-hydroxyarylbis(5-methylfuran-2-yl)methanes a number of by-products were formed. Especially complex mixtures were formed if perchloric acid was used as a catalyst. The complete separation was achieved by column chromatography only. The products structures and transformations sequence are shown on Scheme 1.



**Scheme 1.**

Earlier it has been reported [30] about selective interaction of the reagents **1** and **2** in dioxane in the presence of macroporous highly acid ion-exchange resin Amberlyst-15 with formation of compounds **3**. From our experience this catalyst does not allow to complete the reaction without subsequent transformations. Thus, the extension of reaction time results in increase of benzofuran derivatives **4** amount, whereas at small duration of reaction the conversion of initial aldehydes **1** is low.

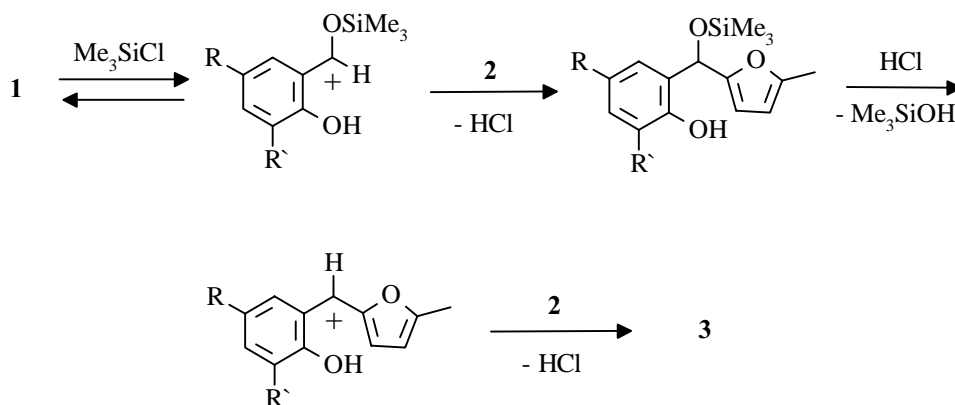
In the course of our work we have found that phenylboric as well as boric acid and boric anhydride are effective in selective transformation **1** into aryldifurylmethanes **3** [31]. The reaction is very selective, since only salicylaldehydes are involved due to intermediate formation of a chelate complex of aldehyde with boric acid (Scheme 2).



**Scheme 2.** X = Ph, OH.

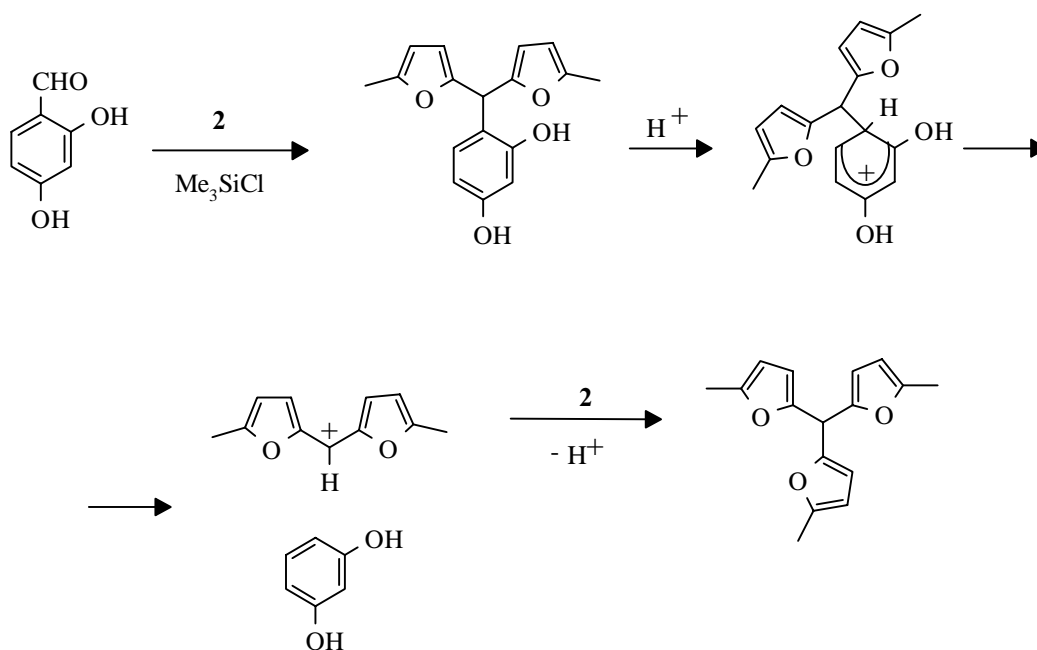
Having advantage in terms of complete absence of tar and by-products in reaction mixture as compared with a perchloric acid, boric acid derivatives have, from another hand, essential drawback - high sensitivity to substituent effects. Satisfactory conversion was reached only in the case of aldehydes **1** bearing withdrawing substituents, while the conversion of salicylaldehyde was 5 % only, and the aldehydes with donor substituents failed to react at all.

Trimethylchlorosilane [31] was recognized as another effective catalyst for mentioned reaction. As it is supposed, the first stage of transformation is a coordination of silicon with carbonyl group of aldehyde in view of high durability of Si-O bond. Formed aryldifurylcarbenium ion is electrophilic enough to attack furan ring through the common electrophilic substitution mechanism.



Scheme 3.

In our opinion,  $\text{Me}_3\text{SiCl}$  is the catalyst of choice for synthesis of compounds **3** since the process is simple, the side reactions are minimized, the yields of 2-hydroxyaryldifurylmethanes **3** are high. It can be used for synthesis with various benzaldehydes.

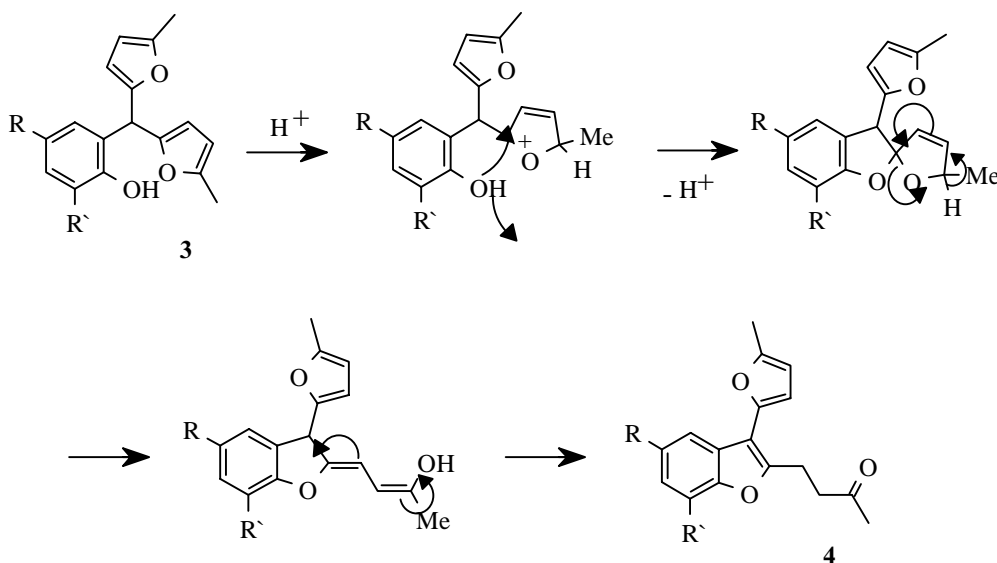


Scheme 4.

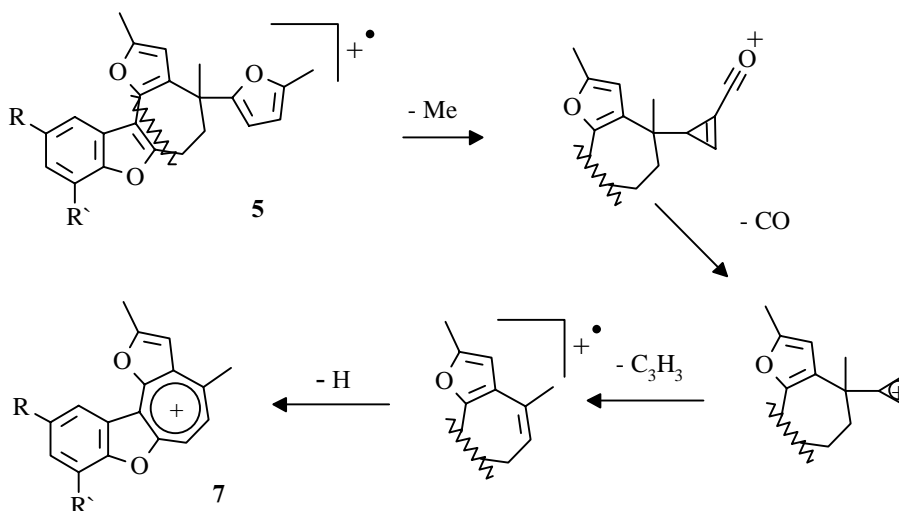
However, attempts to apply  $\text{HClO}_4$  or  $\text{Me}_3\text{SiCl}$  in 2,4-dihydroxybenzaldehyde and 2-methylfuran condensation failed. From this reaction tris(5-methylfuryl)methane was isolated with a high yield (Scheme 4). Apparently, the transformations which are similar to described for 2,4-dimethoxyphenylbis(5-methylfuryl)methane [32,33] take place in this case.

It is supposed that at the first stage initially formed 2,4-dihydroxyphenylbis(5-methylfury-2-yl)methane undergoes protonation by HCl, which is formed during the reaction, and subsequent ipso-substitution leading to resorcinole. Fission of  $\sigma$ -complex results in more stable difurylmethane cation, which quickly reacts with 2-methylfuran giving trifurylmethane. The reaction with 2-hydroxy-1-naphtoic aldehyde proceeds similarly.

The selective transformation of compounds **3** into benzofuran derivatives **4** occurs in ethanol saturated with HCl giving minimum tarification and high yields of the reaction products (Scheme 5) [34].



Scheme 5.

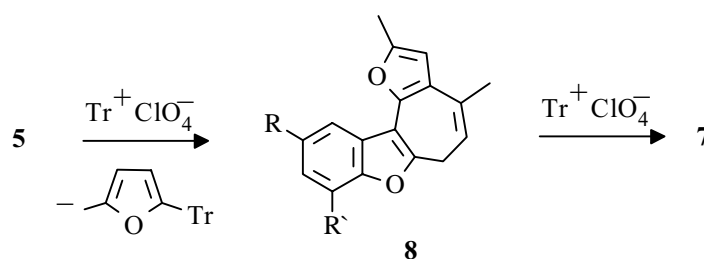


Scheme 6.

Moreover, under these conditions benzofurans **4** can be obtained in one-pot procedure directly from the salicylaldehyde **1** and 2-methylfuran **2**.

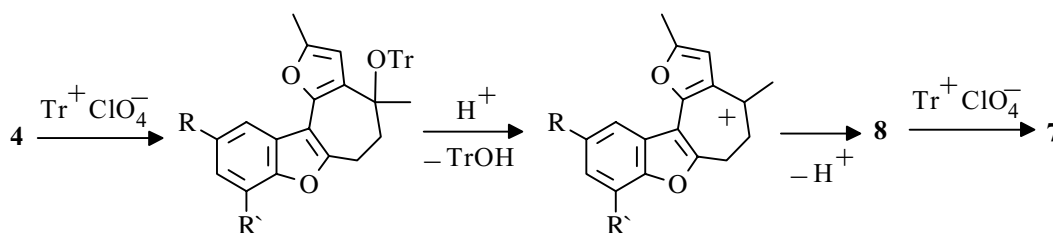
In mass-spectra of compounds **5** occurrence of stable cations **7**, formed in well-known step by step destruction of furan ring (Scheme 6) [29], were observed.

In further studies it was shown that the appropriate benzo[b]furo[2,3-h]-1-oxazulenium salts **7** can be obtained preparatively by treatment of 2-hydroaryldifurylmethanes **3**, benzofurans **4** or compounds **5**, respectively, with tritylperchlorate [35]. The isolation of 5-methylfur-2-yltriphenylmethane from the reaction mixture allowed to suppose that the transformation of pentacyclic compound **5** into perchlorate **7** had occurred via sylvan elimination by tritylperchlorate and subsequent aromatization of formed cycloheptatrienyl derivative **8** (Scheme 7).



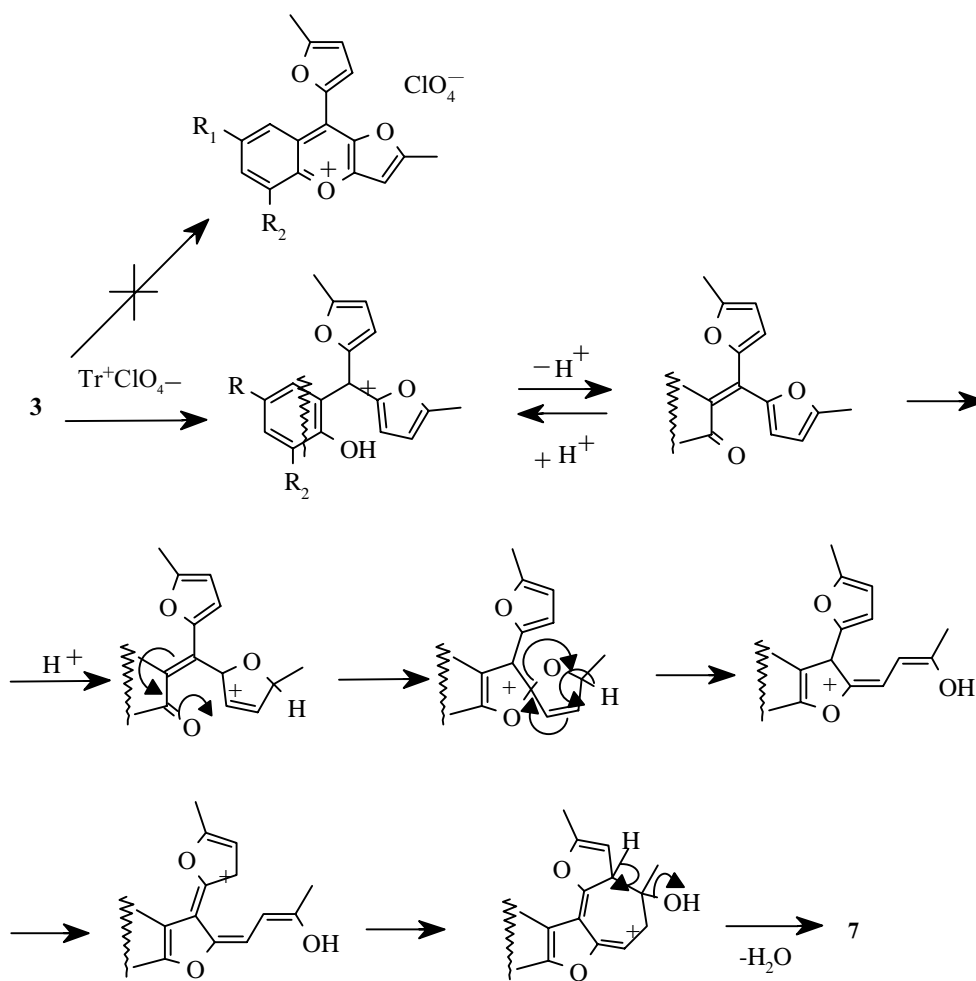
**Scheme 7.**

Formation of salts **7** from the benzofuran derivatives **4**, in our opinion, goes via consecutive stages of the intramolecular cyclization of carbonyl group at  $\beta$ -position of furan cycle, acid catalyzed elimination of triphenylmethanole, resulting in compounds **8**, with further aromatisation by «hydride-ion abstraction» (Scheme 8).

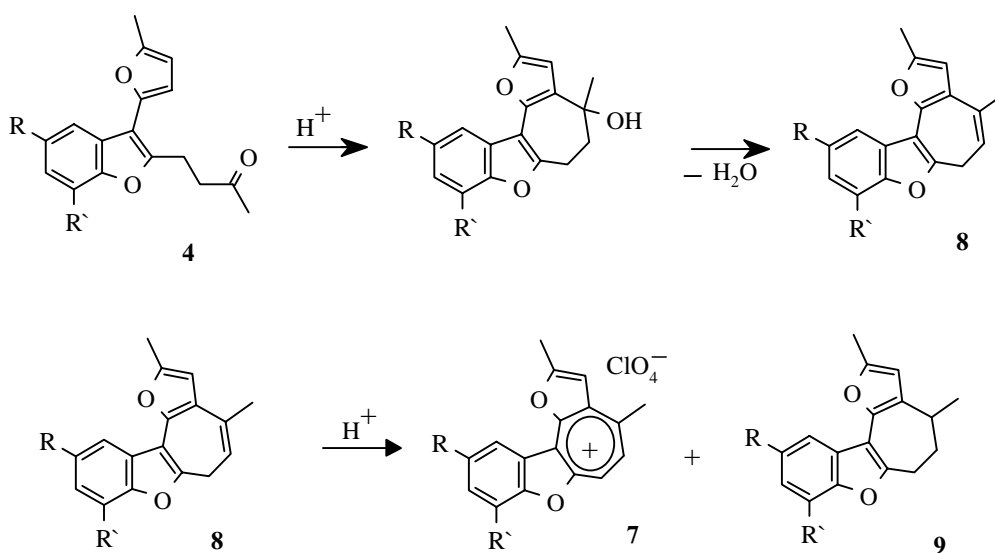


**Scheme 8.**

It is of interest that this reaction pathway is in contrast to that reported for 2-hydroxytriphenylmethanole which gave 9-phenylxanthilium perchlorate under the treatment with tritylperchlorate [36]. In the case of 2-hydroxyaryldifurylmethane **3** apparently the transformation of preliminary formed 2-hydroxyarylbis(5-methylfur-2-yl)carbenium ions has happened (Scheme 9).



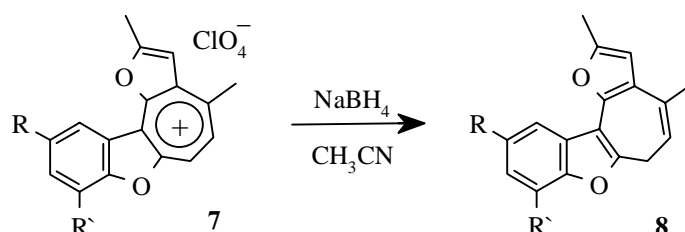
Scheme 9.



Scheme 10.

In our later work [37] it was reported, that refluxing of the benzofuran **4** with perchloric acid in dioxane results in the intramolecular cyclization and the subsequent disproportion of cycloheptatrienyl derivatives **8** to form perchlorates **7** and 5,6-dihydro-2,4-dimethyl-4H-benzo[b]furo[2,3-h]-1-oxazulene derivatives **9** (Scheme 10).

To confirm the scheme of transformations cycloheptatriene derivatives **8** were obtained by the reduction of oxazulonium salts **7** with sodium borohydride (Scheme 11).

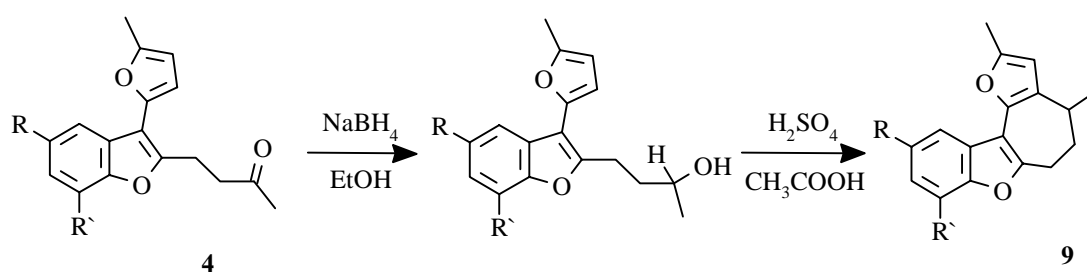


**Scheme 11.**

As expected, the compounds **8** proved to be rather sensitive to air oxygen, darkened at the storage at room temperature and easily formed the appropriate salts **7** with tritylperchlorate. The intermediate formation of the dihydrocompounds **8** in the above mentioned reaction (Scheme 10) was proved by their direct transformation into a mixture of compounds **7** and **9** under the action of equimolar quantities of perchloric acid.

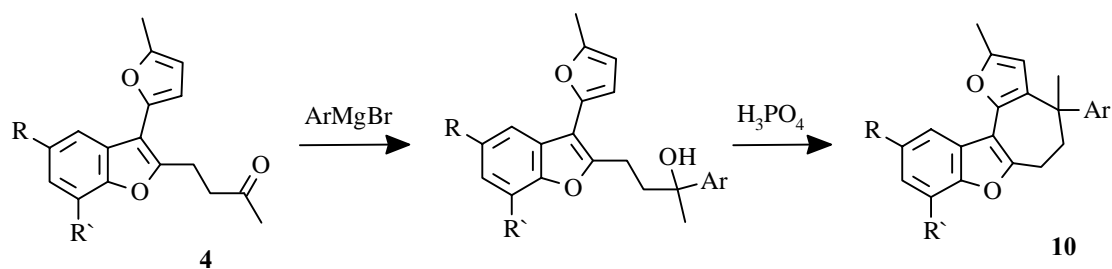
We showed that it is possible to obtain perchlorate **7** directly from salicylic aldehydes **1** and 2-methylfuran **2** by refluxing them in dioxane with perchloric acid.

Dihydroderivatives **9** were obtained by counter synthesis by reduction of appropriate benzofuran ketones to secondary alcohols with the subsequent intramolecular cyclization in the presence of sulfuric acid (Scheme 12) [37].



**Scheme 12.**

Aromatic analogues of compounds **5** were synthesized by phosphoric acid catalysed cyclization of tertiary alcohols resulted from treatment of benzofurans **4** with corresponding arylmagnesium bromides as shown on the Scheme 13.



**Scheme 13.** Ar = phenyl; p-anisyl; o-anisyl.

Thus, starting from the compounds **1** and **2**, it is possible to obtain 2-hydroxyaryldifurylmethanes **3**, benzofurans **4** or oxazulene derivatives **7**, **9** with high selectivity by simple change of the catalyst and solvent.

## References and Notes

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*Samples Availability:* Available from MDPI.