

## Electronic properties of complexes derived from imidazolium cations and carbonyl compounds and their reactivity in synthesis of bisphenol derivatives in the light of CDFT/MEDT approach

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### CHRONICLE

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### ABSTRACT

In terms of Domingo terminology, complexes of carbonyl compounds with imidazolium cations should be considered as extremely strong electrophiles. Reactions of these compounds with phenol yielding bis-phenols follow a polar mechanism. Furthermore, the discussion based on the theory of reactivity indexes can be used to predict the reactivity of respective electrophiles and regio-orientation in EAS reactions, the first stage of bis-phenol synthesis, kinetically rate-limiting for the whole process.

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## 1. Introduction

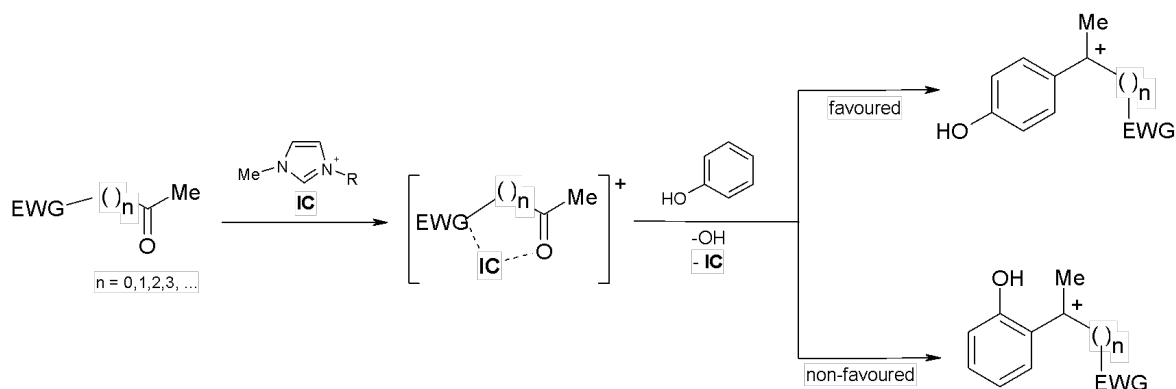
This work is a continuation of our systematic studies<sup>1-4</sup> about effective synthesis of bisphenol derivatives. Bis(hydroxyphenyl)alkyl carboxylic acids and their esters are used for making special purpose polymers. They also improve many of the parameters of the materials produced on their basis. Bisphenols are made by the condensation of phenols with ketoacids or their esters. They are used in production of polyesters, polyethers, polycarbonates and polysulfones, as well as epoxy resins<sup>5-19</sup>. Due to the presence of a carboxyl group, the bisphenol monomer simultaneously fulfills the role of cross-linking compound and a foaming agent. By varying the temperature, it is possible to control the decarboxylation reaction, which allows producing foams with suitable parameters<sup>20,21</sup>. Outside of the plastics industry bisphenols find applications in medicine<sup>22,23</sup>.

The reaction used in synthetic practice which finally yields bisphenol analogues proceeds according to a multi-stage mechanism and the final products are generally bis-(4-hydroxyphenyl)-methylene and (4-hydroxyphenyl)-(2-hydroxyphenyl)-methylene derivatives<sup>1-3,24</sup>. Reactions, such as between phenol and levulinic acid esters follow this pathway; as proved<sup>1,24</sup>, they are catalysed by ionic liquid cations, quite popular recently<sup>25-28</sup>.

It has been proved using kinetic studies<sup>29</sup> that the course of reactions between electrophilic reagents and phenol determines the first stage of an electrophilic attack on the phenol aromatic ring which follows the electrophilic aromatic substitution (EAS) mechanism. In ionic liquid cation-catalysed reactions of imidazolium liquids (IC), this should lead to the formation of benzyl cations as intermediates:

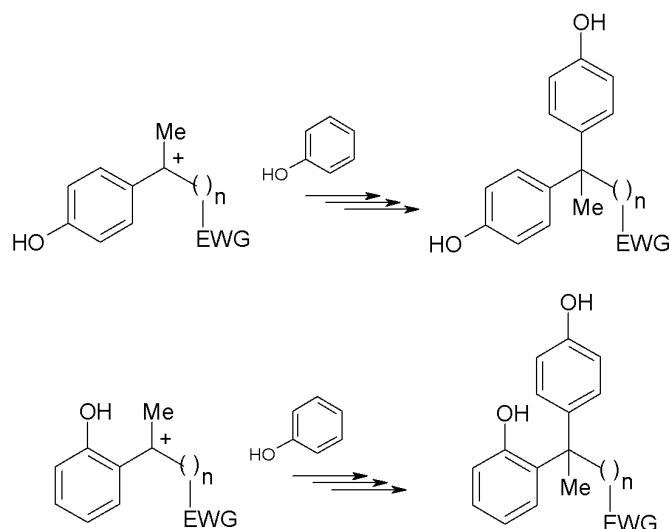
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**Scheme 1.** Reaction course of electrophilic reagents and phenol under EAS mechanism.

The second stage will be more rapid with its course being determined by steric effects which force second substitution in the para position<sup>1-3,24</sup>:



**Scheme 2.** Second stage of the substitution reaction.

Within the investigation, we decided to: (i) evaluate electronic properties of certain electrophiles (derivatives of selected carbonyl compounds) and determine the effect of their structure on reactivity; subsequently, based on the results, (ii) interpret the course of the reaction at a stage which determines OH group orientations in the final adduct. We decided to use the currently widely promoted<sup>30-32</sup> theory of reactivity indexes. Recently this approach has been used successfully to explain the course of a number of bimolecular reactions<sup>30-34</sup>.

## 2. Computational methodology

The quantum-chemical calculations were performed on the Ares computer in the Cracow Computing Center "CYFRONET" using GAUSSIAN 2009 package<sup>35</sup> and B3LYP/6-31G(d) theoretical level. FOPT procedure was applied for the structure optimization of the reactants. Calculations of all critical structures were performed for the temperature  $T=298$  K and pressure  $p=1$  atm. The global reactivity indexes were estimated according to the equations recommended by *Parr* and *Yang*<sup>36</sup> and *Domingo*<sup>30</sup>. In particular, the electronic chemical potentials ( $\mu$ ) and chemical hardness ( $\eta$ ) of the reactants were evaluated in terms of the one electron energies of FMO:

$$\mu = (E_{\text{HOMO}} + E_{\text{LUMO}}) / 2 \quad (1)$$

$$\eta = E_{\text{LUMO}} - E_{\text{HOMO}} \quad (2)$$

The values of  $\mu$  and  $\eta$  were then used for calculation of the global electrophilicity ( $\omega$ ) according to the formula:

$$\omega = \mu^2 / 2\eta \quad (3)$$

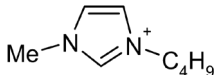
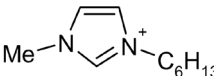
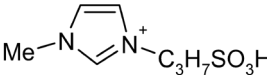
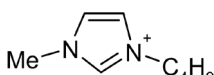
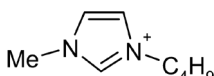
The maximum amount of electronic charge that the electrophile system can accept ( $\Delta N_{\text{max}}$ ) was calculated using the following expression:

$$\Delta N_{\max} = \mu / \eta$$

(4)

Results from calculations were collected in **Table 1**.

**Table 1.** Global electronic properties for electrophilic compounds **1-8**

Nr	Electrophile		$\mu$ [a.u.]	$\eta$ [a.u.]	$\omega$ [eV]	$\Delta N_{\max}$ [e]
	Carbonyl compound	Imidazolium cation				
1	Methyl levulate	-	-0.1323	0.2344	1.02	0.56
2	Methyl levulate		-0.2536	0.1897	4.61	1.34
3	Methyl levulate		-0.2530	0.1904	4.57	1.33
4	Methyl levulate		-0.2379	0.1541	5.00	1.54
5	Nitroacetone	-	-0.1766	0.2111	2.01	0.84
6	Nitroacetone		-0.2887	0.2022	5.61	1.43
7	Nitroacetophenone	-	-0.1778	0.1978	2.18	0.90
8	Nitroacetophenone		-0.2664	0.1740	5.55	1.53

### 3. Results and discussion

We started with the analysis of reactivity of the levulinic acid ester (**1**) tested recently as a component in a reaction with phenol<sup>1,24</sup>. As shown in Table 1, the value of global electrophilicity of levulinate **1** is as low as 1.02 eV. Therefore, according to Domingo's terminology<sup>30</sup>, it should be considered a moderate electrophile. That makes it clear why levulinic acid ester cannot react with arenes without catalysts, even arenes activated by electron-donor substituents.

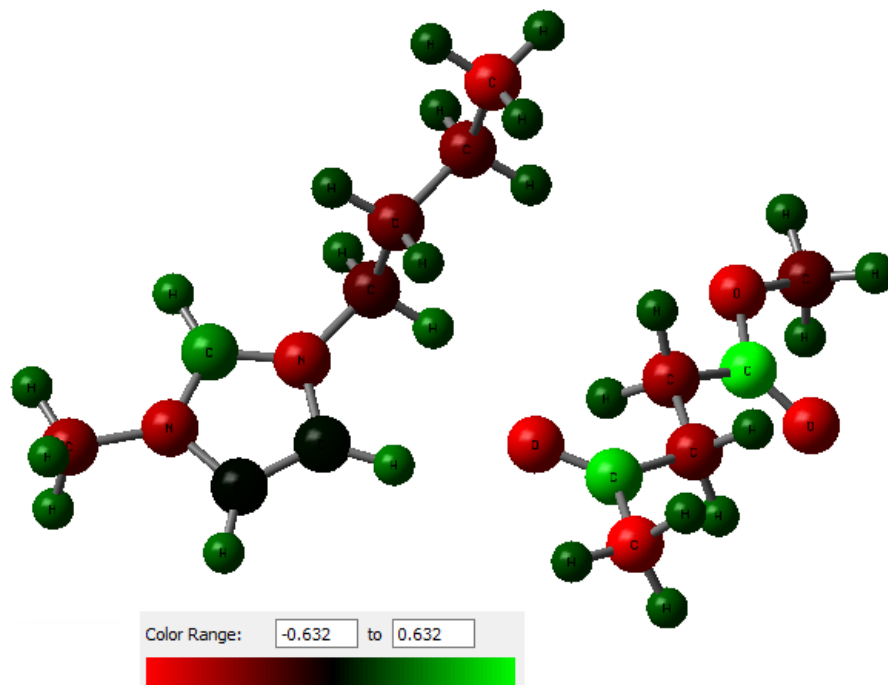
It is known<sup>27</sup>, however, that alkyl levulinates readily form complexes with imidazolium cations. Such complexation should provide significant activation of the electrophile. It was indeed proved that the complex of methyl levulinate with the 1-butyl-3-methyl-imidazolium cation (**2**) has a global electrophilicity value of 4.61 eV, which is higher than that of *gem*-dinitroethene ( $\omega=3.56$  eV<sup>37</sup>), a highly reactive reagent. The reactivity of a complex of ester **1** with the 1-hexyl-3-methylimidazolium cation should be similar. A complex of methyl levulinate with the 1-(3-sulfonylpropyl)-3-methylimidazolium cation (**4**) will be much more electrophilic ( $\omega=5.00$  eV). The maximum charge to be accepted by the electrophile is approximately 1.34 e for complexes **2** and **3** and exceeds 1.5 e for complex **4**, the most electrophilic in the group.

The increase in the reactivity of other carbonyl compounds: nitroacetone (**5**) and nitroacetophenone (**7**) due to complexation with imidazolium ions can be similarly analysed (see Table 1). If used in reactions with phenol, such compounds would potentially enable easy incorporation of a nitro group in the final molecule, and the NO<sub>2</sub> group is known to be a highly universal moiety for further functionalisation<sup>38</sup>. Uncomplexed nitroacetone (**5**) was proved to have a global electrophilicity of 2.01 eV, and 2.18 eV for nitroacetophenone (**7**). Their complexes with the 1-butyl-3-methyl-imidazolium cation (**6** and **8**, respectively) are even stronger electrophiles than similar methyl levulinate complexes ( $\omega>5.5$  eV). The maximum charge to be accepted by the electrophiles exceeds 1.4 e.

Using information on the electronic properties of the electrophiles, we could attempt to interpret the reaction course. Therefore, nucleophilic properties of phenol had to be characterised. This was investigated by Domingo et al.<sup>33</sup>. The authors proved global electrophilicity index  $\omega$  for phenol to be as low as 0.73 eV. Nonetheless, it is a strong nucleophile ( $N=3.16$  eV).

The analysis of chemical electron potentials of the reactants in the reactions (**2-4,6,8** and phenol) confirms that electron transfer in the elementary reaction should occur from phenol ( $\mu=-0.1088$  a.u.<sup>33</sup>) to the carbonyl compound/imidazolium cation complex ( $\mu=-0.2530 \div -0.1766$  a.u.). The comparison of global electrophilicity of the reagents ( $\Delta\omega$ ) provides data

about the driving force of the reactions (Table 2).  $\Delta\omega$  for reactions involving levulinic acid ester complexes exceeds 3.5 eV. Therefore, according to Domingo's terminology<sup>30</sup>, the reactions can be considered strongly polar. In the framework of the theory of reactivity indexes, reactions of methyl levulinate complexes with imidazolium cations (**2-4**) should proceed easily in mild conditions, as proved by experimental data<sup>1,24</sup>. However,  $\Delta\omega$  for nitroacetone and nitroacetophenone complexes is even higher: 4.88 and 4.82 eV, respectively. This means that phenol reactions with complexes of  $\alpha$ -nitro- $\beta$ -carbonyl compounds should proceed even more readily than with methyl levulinate complexes. Soon, we will investigate the reactivity of such complexes experimentally in detail.



**Fig. 1.** View of the model complex between methyl levulinate and methyl-butyl-imidazolium cation with the distribution of Mulliken charges along the molecular segment.

**Table 2.** Differences between global electrophilicity of phenol and electrophilic complexes **2-4, 6, 8**

Electrophile	$\Delta\omega$ [eV]
<b>2</b>	3.88
<b>3</b>	3.84
<b>4</b>	4.27
<b>6</b>	4.88
<b>8</b>	4.82

Finally, the analysis of local phenol nucleophilicity provides information about reagent orientations in the reaction. As Domingo et al. proved<sup>33</sup>, the para position with respect to the hydroxy group is the most active reaction centre in the molecule (local nucleophilicity of 0.85 eV). This position should be preferred in EAS reactions as confirmed by experimental results for processes involving levulinate esters<sup>1,24</sup>. The ortho position is less nucleophilic (local nucleophilicity of 0.38 eV<sup>33</sup>); therefore, the reaction channel leading to (4-hydroxyphenyl)-(2-hydroxyphenyl)-methylene derivatives is less preferred. The meta position is the least nucleophilic reaction centre in phenol (local nucleophilicity of 0.17 eV<sup>33</sup>), and products which could form in an electrophilic attack on that centre do not occur at all.

The course of analogous reactions involving acetone and acetophenone complexes can be predicted similarly. In either case reaction products should be respective bis-(4-hydroxyphenyl)-nitromethylene derivatives.

#### 4. Conclusion

Complexes of carbonyl compounds with imidazolium cations are considered extremely strong electrophiles. Reactions of the electrophiles with phenol yielding bis-phenols follow a polar mechanism. This is confirmed by the analysis of global properties of reaction components. Furthermore, the discussion based on the theory of reactivity indexes can be used to predict the reactivity of respective electrophiles and regio-orientation in EAS reactions, the first stage of bis-phenol synthesis, kinetically rate-limiting for the whole process.

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