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SELECTIVITY IN ELECTROPHILIC ATTACK ON AMBIDENTAL AROMATIC IONS : SYNTHESIS OF 2,2'-DIHYDROXYTRIPHENYLMETANES

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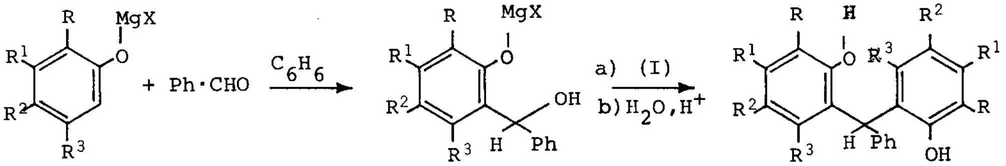
In contrast to what is generally accepted[1], we have recently proved[2] that, under particular reaction conditions, the reactivity of an ambident system in an ion pair, can be enhanced by increasing the coordinating power[3] of the cationic counterion.

Now, we have studied the reactivity of various ambident systems with several electrophilic reagents[4].

In the present work we report the reaction of phenoxymagnesium halides with benzaldehyde which form the 2,2'-dihydroxyderivatives of triphenilmethane (II) previously almost completely unknown.

A selective attack at the ortho position to the phenoxy group was observed in all the cases studied[5,6]. Benzyl alcohol (III), the hypothetical reaction intermediate, reacts quantitatively with the aryloxymagnesium halides to form only one of the possible isomers: the 2,2'-dihydroxytriphenilmetanes (II).



(I) (III) (II)

		R	R^1	R^2	R^3
I_a	II_a	H	H	H	H
I_b	II_b	Me	H	H	H
I_c	II_c	H	H	Me	H
I_d	II_d	Pr^i	H	H	H
I_e	II_e	H	H	Pr^i	H
I_f	II_f	Bu^t	H	H	H
I_g	II_g	H	H	Bu^t	H
I_h	II_h	Me	H	Me	H
I_i	II_i	Pr^i	H	H	Me
I_l	II_l	Me	H	H	Pr^i
I_m	II_m	H	H	OMe	H
I_n	II_n	C_4H_4		H	H
I_o	II_o	H	C_4H_4		H

Reaction of aryloxymagnesium bromides with benzaldehyde[†]

Phenol	Product	Yield %[††]	m.p. °C	δCH[†††]
I_a	II_a	53	128-129	6·10
I_b	II_b	74	127-128	5·88
I_c	II_c	80	oil	5·90
I_d	II_d	100	103-104	5·85
I_e	II_e	93	oil	5·90
I_f	II_f	100	126-128	5·70
I_g	II_g	79	oil	6·00
I_h	II_h	69	107-108	5·88
I_i	II_i	87	112-113	5·88
I_l	II_l	5	oil	5·70
I_m	II_m	78	130-132	5·90
I_n	II_n	100	172-174	5·75
I_o	II_o	100	182-183	5·70

[†] **Refluxed** in benzene for 20 hr; mole ratios ArOMgBr : C_6H_5CHO = 1 : 1.

[††] The remainder of the 100% is constituted of non reacted phenol.

[†††] Chemical shift of the methinic proton registered at 60 Mc in $CDCl_3$.

The importance in these reactions of the acid character and of the coordinating power of the cation is in agreement with the lack of reactivity of the Na^+, Li^+ and Mg^{++} phenolic salts, compared to the high reactivity of the corresponding magnesium halides.

Table 1

Cation effect on the reaction of same phenol salts with benzaldehyde[†]

Reagent	Cation	Phenol reacted %
Phenol[*]	H^+[§], Na^+, Li^+, Mg^{++}	0·0
Phenol[*]	$MgBr^+$	53
o-Tertbutylphenol[¶]	Na^+, Li^+	0·0
o-tertbutylphenol[¶]	$MgBr^+$	80
Resorcinol[¶]	H^+, Na^+	trace
Resorcinol[¶]	$MgBr^+$	68

[†] All the reactions have been conducted in refluxing benzene. Mole ratios ArOMgBr : C_6H_5CHO = 1 : 1.

[*] Reaction time: 20 hr.

[§] Also in the presence of stoichiometric quantities of $MgBr_2$ and $MgCl_2$.

[¶] Reaction time: 3 hr.

It is quite significant the fact that the ortho-disubstituted

2,6-dimethylphenoxymagnesium bromide does not react, while the ortho,para-disubstituted isomer (I_h) is highly reactive.

These data support the hypothesis of a reaction mechanism which involves an electrophilic attack, catalysed by a Lewis acid coordinated both with the reagent and with the phenoxy function of the substrate. For this reason the attack is selective towards the ortho-position.

The lack of reactivity of phenol with benzaldehyde in the presence of $MgCl_2$ and $MgBr_2$, shows at the same time the importance of the basicity of the substrate. This strong sensitivity of the reaction to electronic factors is shown by the *inertia* of chlorophenols and by the increased reactivity observed in the case of particularly basic substrates, such as resorcinols.

The influence of the catalytic action of the counterion[7], however, is also clearly shown in this case: both resorcinol and its sodium salt are much less reactive than the corresponding magnesium bromide.(Tab. 1).

From a preliminary study it was found that the aryloxymagnesium halides also react selectively in the ortho-position with the aliphatic aldehydes, their corresponding acetals and α,β-unsaturated aldehydes.

From a synthetic point of view, these new reactions are the first procedures to bring about electrophilic attacks selectively in the ortho-position to a phenoxy function by aliphatic and aromatic aldehydes[8].

Although from a general point of view these reactions present a mechanism of the Friedel-Crafts type[9], they represent at the same time a new and distinct class within it: the high selectivity of attack in the ortho-position to the phenoxy function, and the possibility of reaction with basic substrates without inactivation of the catalyst are the main peculiarities of these processes.

References and notes

[1] R. Gompper, *Angew. Chem. Int. Ed.* 3, 560 (1964).

[2] B Cardillo, G. Casnati and A. Pochini, *Chimica e Industria* 49, 172 (1967).

[3] The coordinating power can be modified by verying the nature of the reaction medium. See reference 2.

[4] B. Cardillo, G. Casnati and A. Pochini, *Chimica e Industria* 49, 630 (1967).

[5] The yields are almost quantitative on the phenol reacted.

[6] The compounds isolated by simple crystallisation (or distillation) from the reaction mixture (after removal of the non reacted phenol and aldehydes by steam distillation) give analytical data and spectrographs which are completely in agreement with the proposed structure: the ortho-substitution was determined on the basis of the n.m.r. spectra, and by comparison with the para-substituted derivatives. In the n.m.r. spectrum the chemical shift of the methinic proton in the 2,2'-dihydroxysubstituted derivatives is at 5·70-6·10, in the 4,4'-dihydroxysubstituted derivatives at 5·30-5·50, and in the 2,4'-dihydroxysubstituted derivatives at 5·50-5·60δ.

[7] The cationic counterion is not necessarily $MgBr^+$. A Schlenk type or associations equilibria could occur in the system.

[8] The reactions of aldehydes and ketones with phenols, catalysed by protic or Lewis acids, form mainly a mixture of di- or triphenylmethane derivatives in which products from the para attack prevail. G. Olah, *Friedel-Crafts and related reactions*, vol. II, part 1, page 597 (1964), Interscience Publ.

[9] These processes are to be ascribed to a Friedel-Crafts reaction: an electrophilic attack on a basic substrate catalysed by a Lewis acid occurs.