

LCAO HMO STUDY OF THE REACTIVITY OF CHALCONES

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The indices of reactivity for 49 substituted chalcones of benzene and ferrocene type were determined by HMO method and confronted with experimental data on nucleophilic additions and electrophilic substitutions of chalcones and with the data on energies of hydrogen bonds between the chalcones and phenol. The half-wave potentials of polarographic reduction of the chalcones were correlated with the corresponding quantum-chemical data. The structure effects on the reactivity of the chalcones are discussed.

The compounds of type of chalcone $\text{Ar}-\text{CH}=\text{CH}-\text{CO}-\text{Ar}'$ are α,β -unsaturated ketones, which reflects also in their chemical properties. The most reactive site of the molecule is the system $-\text{CH}=\text{CH}-\text{CO}-$. The double bond between the alpha and beta carbon atom easily undergoes addition reactions. The effect of the structure on the reactivity of chalcones in the addition reactions can be satisfactorily described by the Hammett relation¹⁻³. The polarographic reduction of chalcones takes place on the ethylenic group⁴, too.

The oxygen atom becomes the reaction site in the hydrogen bond formation between chalcones and phenol. The energies of these hydrogen bonds correlate well with Hammett's constants^{5,6} and provide some information on the basicity of chalcones.

To date little attention has been paid to electrophilic substitution reactions of chalcones, which take place on the aromatic part of their molecule and the course of which depends on the nature of the aromatic groups Ar and Ar'⁷⁻⁹.

The aim of this work was to contribute to the study of chalcones by quantum-chemical interpretation of their reactivity. In a subsequent paper the quantum-chemical data on chalcones will be extended to the study of π -electron structure in the ground and excited state by semiempirical methods. In this study we chose the chalcones of types A-D as model compounds.

CALCULATIONS

The calculations were made by LCAO HMO method. The Coulomb and exchange integrals were defined in the usual manner

$$\alpha_X = \alpha_0 + h_X \beta_0 \quad \text{and} \quad \beta_{CX} = k_{CX} \beta_0.$$

The values of the empirical parameters h_X and k_{CX} are given in Table I. Localization energies were calculated according to Koutecký¹⁰. In the chalcones of ferrocene type the ferrocenyl rest was considered as cyclopentadienyl anion (*cf.* the model in ref.¹¹).

TABLE I
Parameters for Coulomb and Exchange Integrals of Heteroatoms²².

Substituent	<i>i</i>	<i>j</i>	h_i	k_{ij}
=O	O	C	2.0	1.4
-N(CH ₃) ₂	N	C	1.0	0.8
-NH ₂	N	C	1.5	0.8
-F	F	C	2.5	0.5
-Cl	Cl	C	2.0	0.4
-Br	Br	C	1.5	0.3
-C≡N	N	C	0.5	1.4
-NO ₂	C	N	0.2	1.0
	N	O	1.0	1.0
	O	-	1.5	-
-CH ₃ ^a				
C _α -Y-Z	C _α	Y	-0.1	0.8
	Z	Y	-0.5	3.0
-O-CH ₃	O	C	1.9	0.8

^a Hyperconjugative model.

RESULTS AND DISCUSSION

Addition and Substitution Reactions

Michael addition of ethyl α -cyanobutyrate to chalcones is the first-order reaction in a chalcone³. According to Ingold¹² the rate-determining step of the reaction consists of the attack of the anion of the reagent on the β -carbon atom of the chalcone. It is thus justifiable to correlate $\log k$ with the indices of reactivity calculated for nucleophilic reaction on the β -carbon of the chalcone. The calculated values of S_n and A_n for this carbon atom are summarized in Table II. The correlation of $\log k$

TABLE II

Superdelocalizabilities (S_n) and Localization Energies (A_n) for Nucleophilic Reactions on β -Carbon of Chalcones. Energies of the Lowest Unoccupied Molecular Orbital (LFMO), and π -Electron Densities (q_0) on the Oxygen of Chalcone Carbonyl Group

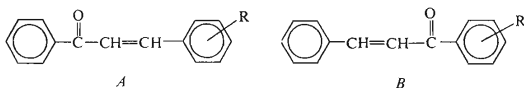
Compound	R	S_n, β^{-1}	A_n, β	—LFMO, β	q_0
Type A					
1	<i>p</i> -N(CH ₃) ₂	2.331	1.804	0.272	1.709
2	<i>p</i> -NH ₂	2.411	1.796	0.262	—
3	<i>p</i> -OCH ₃	2.448	1.810	0.258	1.705
4	<i>p</i> -CH ₃	2.591	1.778	0.238	1.701
5	H	2.609	1.774	0.236	1.700
6	<i>p</i> -F	2.559	1.780	0.243	1.702
7	<i>p</i> -Cl	2.569	1.780	0.242	1.701
8	<i>m</i> -Cl	2.610	1.776	0.237	1.700
9	<i>m</i> -NO ₂	2.610	1.774	—	—
10	<i>p</i> -Fc ^a	2.396	1.804	0.255	—
11	<i>m</i> -Fc	2.611	1.772	0.237	—
12	<i>p</i> -CN	2.749	1.776	—	—
Type B					
1'	<i>p</i> -N(CH ₃) ₂	2.373	1.800	0.264	1.710
2'	<i>p</i> -NH ₂	2.438	1.790	0.257	—
3'	<i>p</i> -OCH ₃	2.394	1.844	0.253	1.705
4'	<i>p</i> -CH ₃	2.594	1.776	0.238	1.701
5'	H	2.609	1.774	0.236	1.700
6'	<i>p</i> -F	2.565	1.782	0.242	1.702
7'	<i>m</i> -OCH ₃	2.610	1.778	0.237	1.700
8'	<i>p</i> -Cl	2.574	1.776	0.241	1.701
9'	<i>p</i> -Br	2.583	1.778	0.240	1.701
10'	<i>m</i> -Cl	2.609	1.772	0.237	1.700
11'	<i>m</i> -Br	2.609	1.774	0.237	1.700
12'	<i>m</i> -NO ₂	2.608	1.774	—	1.700
13'	<i>p</i> -Fc	2.433	1.794	0.251	—
14'	<i>m</i> -Fc	2.610	1.774	0.237	—
Type C					
1	<i>p</i> -OCH ₃	1.942	1.868	0.349	1.728
2	<i>p</i> -CH ₃	2.013	1.857	0.326	1.726
3	H	2.022	1.853	0.325	1.726
4	<i>p</i> -F	1.997	1.858	0.332	1.726
5	<i>p</i> -Cl	2.002	1.856	0.331	1.726
6	<i>m</i> -Cl	2.022	1.856	0.325	1.726
7	<i>p</i> -CN	2.084	1.858	0.283	—

TABLE II
(Continued)

Compound	R	S_n, β^{-1}	A_n, β	$-LFMO, \beta$	q_0
Type C					
8	<i>m</i> -NO ₂	—	—	—	1.726
9	<i>p</i> -Fc	—	—	0.341	1.730
10	<i>m</i> -Fc	—	—	0.325	1.726
11	<i>p</i> -NO ₂	—	—	—	1.721
Type D					
1'	<i>p</i> -OCH ₃	1.857	1.886	0.377	1.725
2'	<i>p</i> -CH ₃	1.910	1.876	0.357	1.723
3'	H	1.917	1.874	0.356	1.722
4'	<i>p</i> -F	1.917	1.874	0.356	1.722
5'	<i>p</i> -Cl	1.901	1.878	0.361	1.723
6'	<i>m</i> -Cl	1.917	1.870	0.356	1.787
7'	<i>m</i> -OCH ₃	1.917	1.874	0.357	1.722
8'	<i>p</i> -Br	1.905	1.878	0.360	1.723
9'	<i>m</i> -Br	1.916	1.868	0.356	1.722
10'	<i>m</i> -NO ₂	1.916	1.876	—	1.722
11'	<i>p</i> -Fc	—	—	0.369	1.728
12'	<i>m</i> -Fc	—	—	0.357	1.722

^a Fc stands for ferrocenyl.

of the above reaction³ with nucleophilic superdelocalizability, S_n , of the chalcones of benzene type is shown in Fig. 1. The analogical correlation for the ferrocene-like chalcones is represented in Fig. 2. It is seen that the correlation is split into separate dependences for individual structure types of the chalcones studied. The same situation has been already found³ for the correlations of $\log k$ with Hammett σ substituent constants, where the slopes of the correlation depended, too, on the type of the chalcones. This may be accounted for by the fact that in the chalcones of types A and B the β -carbon atom on which the reaction proceeds is conjugated *via* benzene ring



with the substituent that affects the rate of the reaction. In the chalcones of types *B* and *D* the substituent is separated from the β -carbon atom by the carbonyl group which acts as partial isolator¹³ and thus restricts the extent to which substituent affects the reaction center. This results in the higher value of the slope of the correlation for the chalcones of types *B* and *D*, even though the difference in the slopes is not so large as in the case of the correlations of the HMO quantities with the experimental data. As in the simple HMO model only π -electrons are considered, it can not give a true picture of the differences in the structure of these compounds (reflected in the

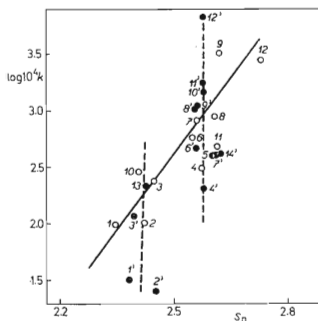
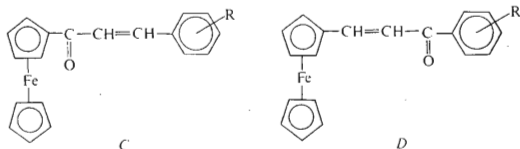


FIG. 1

Dependence of $\log 10^4 k$ of the Addition³ of Ethyl α -Cyanobutyrate to the Chalcones of Benzene Type on Nucleophilic Superdelocalizability S_n

Full line corresponds to the chalcones of type *A* and broken one to the chalcones of type *B*. For numbering of compounds see Table II.

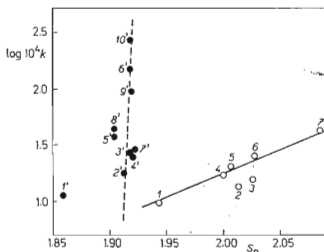


FIG. 2

Dependence of $\log 10^4 k$ of the Addition of Ethyl α -Cyanobutyrate to the Chalcones of Ferrocene Type on Nucleophilic Superdelocalizability S_n

For numbering of compounds see Table II.

experimental data). This manifests itself in an insignificant effect of substituents on the HMO data for the chalcones of types *B* and *D*. The linear dependence for the chalcones of type *B* is further split into two subgroups; the one is formed by the derivatives with strongly electron-donor substituents such as *p*-NH₂, *p*-N(CH₃)₂, *p*-OCH₃ and *p*-Fc. This splitting may originate from the choice of HMO parameters. There is a marked difference between the correlations for the chalcones of benzene and of ferrocene type, the splitting in the latter case being more distinct. The dependences of log *k* on anion localization energy and on β -carbon π -electron density are of similar form.

Electrophilic substitutions on chalcones have been so far studied only in a few cases. Toma⁹ confirmed the reactive positions of some ferrocene analogues of chalcones in electrophilic substitutions by quantum-chemical calculation. The diagrams of cation localization energies A_e of the chalcone, *m*-nitrochalcone of type *B*, and *p*-nitrochalcone of type *A* are represented in Fig. 3. In all the above compounds the lowest value of cation localization energy corresponds to position 1, which indicates that this position is most liable to electrophilic substitution. However, according to Arbusov and coworkers¹⁴, *ortho* positions of chalcones are sterically hindered so that in most cases electrophilic substitutions do not proceed in these positions. From the values of localization energies it is seen that other suitable positions for electrophilic attack are the position 3 in chalcone and *m*-nitrochalcone, and the position 15 in *p*-nitrochalcone. In accordance with this the nitration of the above compounds proceeds in these positions⁷. However, under different reaction conditions the nitration of chalcone yielded a mixture of 1- and 3-nitrochalcone⁸.

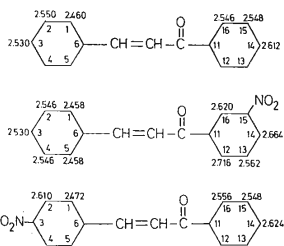


FIG. 3

Diagrammatic Representation of Electrophilic Localization Energies A_e of Chalcone, 15-Nitro- and 3-Nitrochalcone

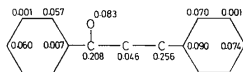
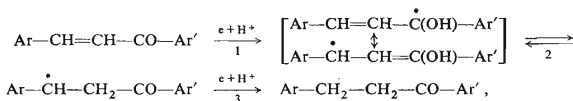


FIG. 4

Diagrammatic Representation of the Squares of Expansion Coefficients of LFMOs of Chalcone

Polarographic Reduction

The first step of polarographic reduction of conjugated compounds involves the transfer of electron from the electrode to the lowest unoccupied π -molecular orbital (LFMO). The value of half-wave potential of polarographic reduction thus becomes proportional to the energy of this orbital. From experimental studies on polarographic reduction of chalcones it follows that the reduction of the C=C bond precedes that of the carbonyl group⁴. The reduction of the ethylenic group consists of the two one-electron steps. For aromatic chalcones the following mechanism of the reduction has been suggested^{15,16}:



where the first stage of the reaction determines the value of the potential. A similar mechanism has also been proposed for the reduction of ferrocene analogues of chalcones¹⁷. Fig. 4 shows the diagram of squares of expansion coefficients (c_j^2) of LFMO of unsubstituted chalcone which determines electron distribution in this orbital.

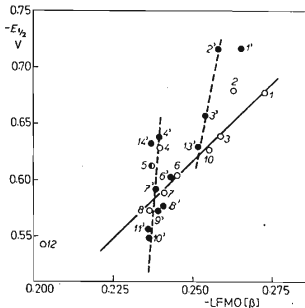


FIG. 5

Dependence of Half-Wave Potentials of Polarographic Reduction of the Chalcones of Benzene Type¹⁸ on LFMO Energies

Full line corresponds to compounds of type A, broken one to compounds of type B.

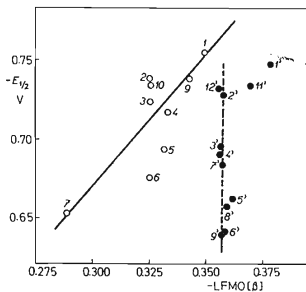


FIG. 6

Dependence of Half-Wave Potentials of Polarographic Reduction of the Chalcones of Ferrocene Type¹⁸ on LFMO Energies

Numbering of compounds is given in Table II.

It is seen that the most probable localization of reducing electron is that on the β -carbon of the ethylenic group and on the carbon of the carbonyl group, which is in accordance with the proposed mechanism of the reduction. Analogical results were obtained also for other chalcones studied.

Calculated LFMO energies for the chalcones studied are given in Table II. Figs 5 and 6 show the correlation of the energies with the values of half-wave potentials measured at pH 2.48 (ref. 18) for the chalcones of types *A* and *B* and of types *C* and *D*, resp. The course of the dependences is similar to that in Figs 1 and 2, which supports the assumption that also here the β -carbon atom becomes the reaction center. The linear correlation for the chalcones of type *B* is again split into two subgroups, quite as in Fig. 1.

Basicity

The energy of the hydrogen bond between the carbonyl group of chalcone and phenol is the measure of the relative basicity of chalcones. Noyce¹⁹ showed that there exists a dependence between the basicity of chalcones and the shift of the wave-number of IR absorption band of phenol O—H stretching frequency ($\Delta\nu(\text{OH})$). The energy of

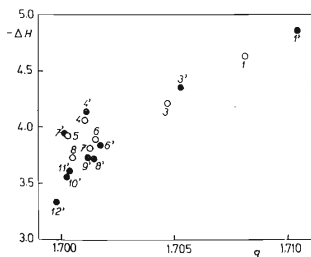


FIG. 7

Dependence of Energies of Hydrogen Bonds ($-\Delta H$) between the Chalcones of Benzene Type and Phenol upon π -Electron Density on the Carbonyl Oxygen

For numbering of compounds see Table II.

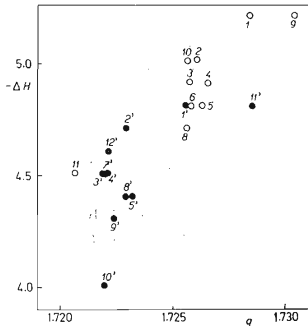


FIG. 8

Dependence of Energies of Hydrogen Bonds ($-\Delta H$) between the Chalcones of Ferrocene Type and Phenol upon π -Electron Density on the Carbonyl Oxygen

For numbering of compounds see Table II.

hydrogen bond between the chalcone carbonyl group and phenol is then defined²⁰ as

$$\Delta H = 0.016\Delta\gamma(\text{OH}) + 0.63.$$

π -Electron density on the carbonyl oxygen may be considered as the suitable quantum-chemical index proportional to the basicity of chalcones. Calculated values of π -electron density on the carbonyl oxygen are given in Table II. Fig. 7 shows the correlation of the energies of hydrogen bonds of chalcones determined by IR spectroscopy^{6,21}. The analogical correlation for the chalcones of type C and D is illustrated in Fig. 8. These correlations differ from those mentioned earlier in that only a relatively small splitting of the data according to the type of the chalcone can be observed. This can be explained by assuming that here the oxygen atom of the carbonyl group, which is directly conjugated with the rest of the molecule, is the reaction center. Another characteristic feature of the correlations in Figs 7 and 8 can be seen in that there are no separate linear regressions for the two types of the chalcones studied and that the experimental data on both the Figures form band.

The difference between π -electron energies of the protonated and free form of chalcone should have been also proportional to the relative basicity of the compounds. The correlations of this quantity with the energy of the hydrogen bond, ΔH , did not yield satisfactory results.

CONCLUSION

The chemical reactivity of chalcones can be satisfactorily interpreted on the basis of quantum-chemical quantities determined by the HMO method. The experimental and calculated quantities yield reasonable correlations. For the reactions taking place on the ethylenic group of chalcones the correlations are split into separate dependences. This splitting is relatively small when the oxygen of the carbonyl group becomes the reaction center. The reaction sites predicted for electrophilic substitution of the aromatic part of selected types of chalcones on the basis of quantum-chemical calculations are confirmed by experimental data. The magnitude of expansion coefficients of LFMO orbital confirms the proposed mechanism of polarographic reduction of chalcones.

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