

QUANTUM CHEMICAL STUDY OF THE EFFECTS OF SUBSTITUENTS ON THE π -ELECTRON STRUCTURE AND REACTIVITY OF CHALCONE

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The SCF CI method in π -electron version was used to study the effect of substituents on the π -electron structure and reactivity of twenty three monosubstituted derivatives of *trans*-chalcone I. Experimental quantities, such as rate constants, polarographic half-wave potentials, dissociation constants, and UV absorption band shifts are compared with corresponding theoretical indices of reactivity.

This work is a continuation of our previous studies^{1,2} on chalcone derivatives. The quantum chemical method employed is suitable for studying these π -systems, since *trans*-chalcones are planar molecules^{3,4} (contingent small deviations from planarity do not affect the properties studied⁵). In such a case π -electron approximation yields relevant information concerning physico-chemical properties of these compounds and their interrelations.

CALCULATIONS

Pariser-Pople-Parr (PPP) method was used with variable β -approximation according to Nishimoto and Forster⁶, where β is a linear function of bond order ($\beta_{ij} = A_0 + A_1 p_{ij}$); $A_0 = -2.0$ for the C—C bond and -2.2 for the C=O bond, $A_1 = -0.51$ for the C—C bond and -0.56 for the C=O bond. The advantage of this method is in that it does not require the knowledge of accurate geometry of molecules. Resonance integrals between substituent and benzene ring carbon were constant. Diagonal elements H_{pp} were approximated by corresponding ionization potentials. In the case of strongly polar σ -bond between a substituent and the carbon of the chalcone skeleton, the ionization potential of the substituent was adjusted empirically^{7,8}. One-center repulsion integrals were expressed by empirical values, bicentric ones were calculated according to Mataga-Nishimoto relation⁹. In configuration interaction, 25 monoexcited configurations were considered. The bond distances between the carbon atoms of the chalcone skeleton were all taken as 1.40 Å, the C=O bond length being 1.23 Å. The benzene rings were regarded as regular hexagons with the bond angles of 120°. The numbering of the atoms adopted is seen in the Scheme. All the parameters used, as well as the geometry of substituents, are summarized in Table I.

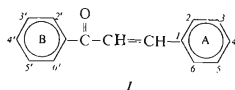
RESULTS AND DISCUSSION

The majority of chemical reactions of chalcones take place on the $-\text{CO}-\text{CH}=\text{CH}-$ group. As its reactivity is to a great extent influenced by distribution of electron density at the reaction centers, we first examined the effect of substituents on the change of charge densities in this group. The calculation revealed that the charge density at carbon 7 is only slightly affected by substituent. Relatively the greatest change was observed upon introduction of $4'\text{-N}(\text{CH}_3)_2$ group ($\Delta q = 0.011$). The charge density at the carbonyl oxygen increases upon introduction of electron-releasing substituents and decreases in the presence of electron-withdrawing groups, the stronger effect being exerted by the substituent attached to ring B. Charge density at carbon 9 depends upon whether the substituent is bonded to ring A or to ring B. In the former case, an electron-releasing substituent increases the charge density, while an electron-withdrawing group exerts the reverse effect. The opposite situation arises if the substituent is attached to ring B; here electron-releasing groups decrease and electron-withdrawing substituents increase the charge density. In the case of carbon 10, electron-releasing substituents on ring A decrease and electron-withdrawing groups increase the charge density. When attached to ring B, the substituents exert opposite effect. In all the cases the substituent exhibits stronger effect from position *para* than from position *meta*. Quantitatively, the strongest electron-releasing group is $-\text{N}(\text{CH}_3)_2$ and the strongest electron-withdrawing group is $-\text{NO}_2$, in accordance with expectation.

TABLE I
Parameters Adopted and the Geometry of Functional Groups^a

Group (atom)	$-W_x$, eV	γ_x , eV	β_{cx} , eV	r_{cx} , Å
C	11.16	11.13	—	1.40
O	17.70	15.23	—	1.23
F	34.46	16.26	-2.67	1.30
Cl	24.02	11.27	-1.86	1.69
Br	19.10	9.26	-1.84	1.86
CH_3^b	29.00	10.00	-5.00	1.50
NH_2	21.30	14.93	-2.30	1.36
$\text{N}(\text{CH}_3)_2$	20.00	13.95	-2.60	1.36
OCH_3	28.00	17.99	-2.11	1.36
NO_2 $\begin{matrix} \nearrow \text{N} \\ \searrow \text{O} \end{matrix}$	24.20	16.60	-1.60	1.48
	15.90	13.90	-2.40	1.21
CN $\begin{matrix} \nearrow \text{C} \\ \searrow \text{N} \end{matrix}$	11.16	11.13	—	1.42
	13.80	12.63	-3.80	1.16

^a All the symbols used have conventional meaning; ^b Hetero atom model of methyl group.



Charge densities of the $-\text{CO}-\text{CH}=\text{CH}-$ group in the first excited state are listed in Table II. It becomes immediately clear that in all the compounds studied the excitation increases charge density at the oxygen and carbons 7 and 10 and decreases the density at carbon 9. Charge density at the oxygen changes upon substitution similarly as in the ground state, *i.e.* an electron-releasing group has the enhancing and an electron-withdrawing substituent the reducing effect. The charge density at carbon 9 increases upon substitution, with the exception of electron-withdrawing substituents on ring B, which bring about the decrease in charge density. Charge density at carbon 10 increases by the effect of an electron-releasing substituent and

TABLE II
SCF π -Electron Charge Densities of the $-\text{CO}-\text{CH}=\text{CH}-$ Group of Substituted Chalcones I in the First Excited State

Substituent	Carbon atom in position			
	7	8	9	10
H	0.897	1.495	0.876	1.009
4-F	0.901	1.507	0.895	1.031
4'-F	0.895	1.503	0.883	1.010
3-Cl	0.899	1.507	0.905	1.025
3'-Cl	0.896	1.499	0.877	1.010
4-Cl	0.899	1.511	0.910	1.039
4'-Cl	0.895	1.511	0.881	1.009
4'-Br	0.897	1.522	1.027	1.066
4-N(CH ₃) ₂	0.909	1.563	1.036	1.105
4'-N(CH ₃) ₂	0.887	1.543	1.127	1.128
4-NH ₂	0.905	1.561	1.041	1.104
3'-OCH ₃	0.892	1.493	0.881	1.010
4-OCH ₃	0.897	1.531	0.966	1.072
4'-OCH ₃	0.896	1.513	1.020	1.064
4-CH ₃	0.908	1.528	0.930	1.065
4'-CH ₃	0.895	1.521	1.036	1.075
3'-NO ₂	0.891	1.485	0.867	0.994
4-NO ₂	0.847	1.464	0.906	0.971
4'-NO ₂	0.879	1.477	0.854	0.974
4-CN	0.870	1.480	0.894	0.994
4'-CN	0.897	1.495	0.864	0.993

decreases upon introduction of an electron-withdrawing one, regardless whether the substituent is attached to ring A or B. Charge density at carbon 7 is increased only by electron-releasing substituents on ring A; in the other cases charge density decreases. From the above results it may be concluded that the excited state is much more sensitive toward substituent effects, the changes of charge densities are significantly greater, relative to the ground state.

A comparison of the experimental with the calculated data on chemical reactivity or equilibria was made on the basis of following reactivity indices obtained from SCF data: charge density, atom localization energy, and free valence.

Correlation of $\log k$ of nucleophilic addition of chalcones studied by Toma¹⁰ with π -electron density at the reaction center is graphically represented in Fig. 1. The correlation is split into two parts, in dependence on the location of substituents. The sensitivity of the reactivity towards the effect of the substituent from ring A and B is practically the same. For comparative purposes, the correlation of $\log k$ of the same reaction with SCF atom localization energy is shown in Fig. 2. The correlation is again very good; the splitting into two parts is not here so distinct.

The properties of the ethylenic group in polarographic reduction of chalcones are seen from the correlation of half-wave potentials of the first reduction step¹¹ with charge density (Fig. 3) and SCF free valence (Fig. 4). We regard this approach as fully justified, since it may be assumed that the reduction process on the surface of the electrode, which is otherwise quite complex¹, involves radical species^{13,14}. As to the course of polarographic reduction of chalcones, several different mechanisms have been suggested¹²⁻¹⁴, some authors assuming the first step to be the reduction in position α with respect to the carbonyl, others the reduction in the β position. For that reason we correlated the data in the above way both for the α - and for the β -carbon of the ethylenic group of chalcones. As it is seen, the correlation of $-E_{1/2}$ with charge density is very good for both carbon atoms and again it consists of two parts. A good correlation exists also between $-E_{1/2}$ and free valence. While in the case of the α position (Fig. 4a) the splitting of the correlation is apparent, only one correlation, with two points outside it, was obtained for the β position (Fig. 4b).

The effect of substituents on the basicity of the carbonyl group is evident from the correlation of pK_{BH} 's of the chalcones with theoretical quantities. According to the relation between pK and the atom charge density obtained on the basis of perturbation theory¹⁵, the dependence of pK_{BH} of the chalcones on charge density at the oxygen should be linear. This is the case (Fig. 5). The existence of simple, linear correlation is the result of equal effect of substituents from both benzene rings. The values of pK_{BH} of substituted chalcones were determined by the method of hydrogen bond¹⁶ on the basis of linear correlation of the basicities of substituted chalcones¹⁷ with the wavenumbers of OH stretching vibration of phenol associated through hydrogen bond with chalcones^{18,19}. Separate correlations were plotted for substituents on rings A and B.

The calculated energies of the transitions in UV spectra of *trans*-chalcones agree very well with experimental data². Substitution affects both the position of the main absorption band and charge density. The difference of the wavenumbers of the parent and substituted chalcone does not correlate directly with charge density at the carbon bearing substituent in the first excited state; it yields, however, a satisfactory correlation (Fig. 6) with the function

$$\log \left(\frac{q_{i,0}^*}{q_i^*} \frac{1 - q_i^*}{1 - q_{i,0}^*} \right),$$

where q_i^* and $q_{i,0}^*$ is the charge density at the carbon bearing substituent and at the carbon of the parent compound, respectively. In this case, the function should express the change of free energy in the excited state caused by substitution. As it is seen from Fig. 6, the correlation consists of two portions, which correspond to the chalcones substituted at rings A or B. The effect of substituents is significant only in the case of the substitution at ring A, while the effect of substituents attached to ring B is negligible, with the exception of the dimethylamino group. The value for 4-nitrochalcone deviates from the correlation.

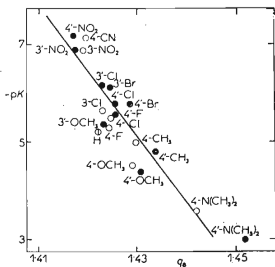


FIG. 5
Correlation of pK_{BH+s} of Chalcones with Charge Density at the Carbonyl Oxygen

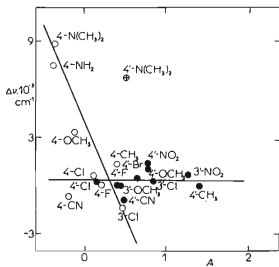


FIG. 6
Correlation of the Differences between the Wavenumbers of the Main Absorption Bands of the Parent Compound and Substituted Chalcones $\Delta\nu$, with a Function of Charge Density in the First Excited State (A)

$$A = \log \left(\frac{q_{i,0}^*}{q_i^*} \frac{1 - q_i^*}{1 - q_{i,0}^*} \right)$$

In conclusion it can be said that the correlation of experimental data on mono-substituted *trans*-chalcones, such as reactivities, chemical equilibria, and UV absorption band shifts, with theoretical quantities are very good and describe well the effect of substituents on the π -electron structure and reactivity of these compounds. The greatest deviations of theoretical from experimental data were observed with strongly polar groups (NH_2 , $\text{N}(\text{CH}_3)_2$). The best quantity for interpreting reactivity turned out to be π -electron charge density, which describes well the different effect of substituents on the reaction center from different sites of the molecule.

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