PROCEEDINGS OF THE YEREVAN STATE UNIVERSITY

Chemistry and Biology 2016, № 3, p. 19–24

Chemistry

CHARGE COMPONENTS OF INDUCTIVE EFFECT OF ALKYL GROUPS AND THEIR INFLUENCE ON THE CHEMOSELECTIVITY OF ALCOHOLS BENZOYLATION

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The inductive effect of alkyl groups of alcohols is an additive quality, which arises because of the differences in electronegativities of atoms of hydrogen, carbon, and oxygen in the molecule of alcohol are provided. Thanks to that a negative charge is formed on carbon atoms of the C–H bond, and a positive charge on carbon atoms of C–O bond. We show that these charges are equivalent to the natural forces of affinity, which cause the chemoselectivity of molecules.

Keywords**:** electronegativity, chemoselectivity of molecules, acid of Pauling, base of Pauling.

It is believed that that the inductive effect of alkyl groups is the property of electron donating, which grows in the homologue sequence corresponding to Me<Et<Pr<Bu etc., extends just to a few (typically 2–3) σ-bonds C–C. However, using the method of competitive reaction experimentally was proved that the effect of alkyl groups on the chemoselectivity of alcohols extends up to 10 σ-bonds C–C [1]. From these facts it becomes obvious that the commonly accepted viewpoint on the threshold of the inductive effect is incorrect. Then a new problem arose, one need to explain the discrepancy between the predictions of the theory and the experimental facts [1–6].

In the present paper some conclusions from the research, explaining these discrepancy, with the examples on the molecules of alcohols are presented. These conclusions, as those presented in [1], were surprising, but connected with each other in a causal relationship. These connections were possible to find by the help of new version of acid-base theory [7, 8]. The main characteristic of this approach is that the interactions of atoms are viewed as interactions of charges, which have a donor-acceptor (acid-base or redox) nature. Thus, for the given case it should be noted that the effect of an alkyl group is an additive property, which is a sum of two effects of opposite charges. One of them comes up thanks to the interaction of atoms on C–H bond, where the hydrogen inducts a negative charge on the carbon atom, and the other comes from the interaction of atoms in the α-C–O bond, where oxygen causes a positive charge on the carbon atom. The qualitative analysis of the

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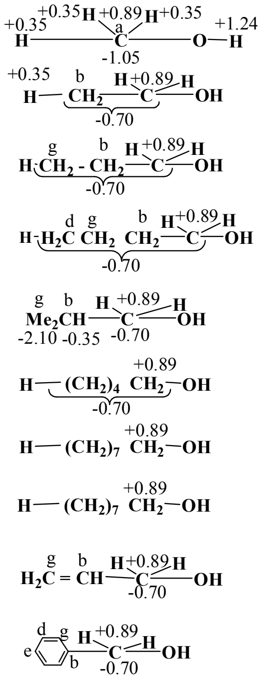
charge distribution on these atoms can be solved easily [7, 8], but two more issues remain. If the chemical reaction is an interaction between particles of opposite charges, then why it does not end with an instantaneous cancellation of the lesser charge? Can the chemical properties of the molecules be explained by the values of the charges that arise on carbon atoms in the alkyl groups? The first of these questions is a result of a far bigger mystery in chemistry. The main issue is the underestimation of the fact that the atoms of the elements are not simply elementary particles of opposite charges, but complex formations, the characteristic charge of which is defined by the interactions with other charged particles and atoms. On the one hand, it is the positive charge of the atom of the reagent (the initiator of the interaction); on the other hand, the opposing forces of negative charge on the atoms of substrate (the source of electrons). Therefore, the strength of the contact of such an acceptor with the atoms that are sources of electrons (bases of Pauling [7, 8]) depends on certain circumstances and does not happen automatically, but after overcoming different opposing forces. For the same reason the cancellation of charges on particles continues not until full neutralization, but until an equilibrium of forces is established. Most importantly, with this information we can estimate both the sign and the value of the charge on the α-atom of carbon, and through it also on the atom of oxygen in the α-C–OH bond as a negative charge of the same value. A thorough solution of the problem is found when taking into account a natural reference point, which for electrons and protons of individual atoms was recently discovered and described [7, 8].

The main essence of the finding is that against the common perception, the positive charge of the nucleus of atoms is neutralized only partially by electrons (except for noble gases). In fact, very often the charge of the nucleus that is not neutralized is bigger than the neutralized portion. Eventually, it is this non-neutralized charge of the nucleus that participates in a chemical reaction (neutralizes), but only during an interaction with electrons of other atoms. This partial charge of the nucleus is called electronegativity by L. Pauling [9].

The aforementioned thoughts bring to a conclusion, the importance of which on theory and synthesis has not been given enough attention yet. If the neutralization of positively and negatively charged particles in the atoms is partial even during such a close contact (within the atom), then with greater separation, such as during intramolecular interactions of charges on atoms in carbon chain of alcohols, this neutralizations will get even smaller.

Of course, it is still hard to estimate the exact degree of this neutralization. But the fact that such a separation will bring to very quick attenuation of the forces of atoms interaction has been mathematically proved [3]. Thereby, it is natural to think of a border of interaction, which would be dependent on the quantity of the charge and the distance, from where the neutralization of α-carbon takes place (Sch. 1). Indeed, taking these into account we managed to find correlations between experimental facts and theoretical predictions. In particular, we can find those, if the expected difference between the atoms of carbon of opposite charges is explained by the difference in distance. For example, our reasoning becomes simple, if we treat the gradation as some portion of the partial charge of α-carbon proportional to distance from it. In other words, in order to estimate the interaction of atoms we can replace the nominal charge on carbon in C–H bond (–0.35 in units of ionic characteristics, u.i.c.) with its portions (–0.035 u.i.c. for β-carbon; –0.0035 u.i.c. for α-carbon, ets.), as shown in Sch. 1. This allows solve two important problems in theory: that is the estimation of the amount of negative charges on α-, β-, and subsequent atoms of carbon, which takes part in interactions and the amount of positive charge that α-carbon takes.



$AF(C)_{C\text{-}O}$= +0.89-0.105= +0.7850.
DF(O) = -0.7850-1.24- = **-2.0250**

$AF(C)_{C\text{-}O}$= +0.89-0.0700-0.0105= +0.8095.
DF(O) = -0.8095-1.24= **-2.0495**

$AF(C)_{C\text{-}O}$= +0.89-0.07805= +0.81195.
DF(O)=-0.81195-1.24=**-2.05195**

$AF(C)_{C\text{-}O}$= +0.89-0.077805= +0.812195 or
+0.89-0.07777-0.000035= +0.812195.
DF(O) =-0.812195-1.24= **-2.052195**.

$AF(C)_{C\text{-}O}$= +0.89-0.0700-0.0035-0.0021= +0.8144.
DF(O) = -0.8144-1.24= **-2.0544.**

$AF(C)_{C\text{-}O}$= +0.89-0.077777-0.0000035=+0.8122195.
DF(O) =-0.8122195-1.24= **-2.0522195.**

$AF(C)_{C\text{-}O}$=+0.89-0.077777777-0.0000000035=+0.8122195.
DF(O) =-0.8122222195-1.24= **-2.0522222195**.

$AF(C)_{C\text{-}O}$=+0.89-0.077777777-0.0000000035=+0.8122195.
DF(O) =-0.8122222195-1.24= **-2.0522222195**.

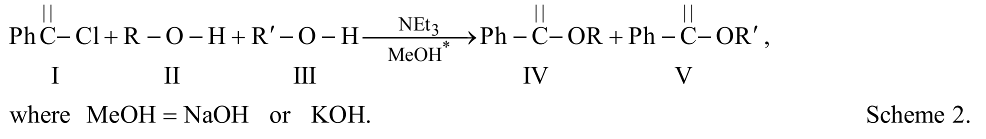
$AF(C)_{C\text{-}O}$= +0.89-0.0700-0.0035 -0.0007-0.0040$*^1$=+0.8118.
DF(O) =-0.8118-1.24= **-2.0518.**

$AF(C)_{C\text{-}O}$= +0.89-0.0707735-0.00444 $*^1$= +0.8147865.
DF(O) = -0.8147865-1.24= **-2.0547865**.

Scheme 1. Pattern of changes of the acceptor force (AF) of carbon atom and the donor force (DF) of oxygen atom of alcohols.

Where 0.35, 0.89 and 1.24 are the ionic characteristics of the bounds C–H (2.55–2.20 = 0.35), C–O (3.44–2.55=0.89) and O–H (3.44–2.20=1.24); 2.20, 2.55 and 3.44 are the electronegativity of hydrogen, carbon, oxygen atoms (u.i.c.) [9]. Nominal values of negative changes of carbon atom in methine, methylene and methyl group are –0.35, –0.70 and –1.05 u.i.c. The value of negative change of carbon atom in the benzene ring equals to –0.40 u.i.c. for absence of substituents.

All of this allows us to differentiate the roles of charge separation in C–H and C–O bonds in determining the chemical nature of a function group (hydroxy group in this case). It becomes obvious that the effect of alkyl group on oxygen in hydroxy group happens not through the simple mechanism of transferring the donor force (i.e. without taking into account the effect of oxygen on α-carbon) in particular, which is accepted in [2–6], but as a result of interaction between oppositely charged atoms [7–8].

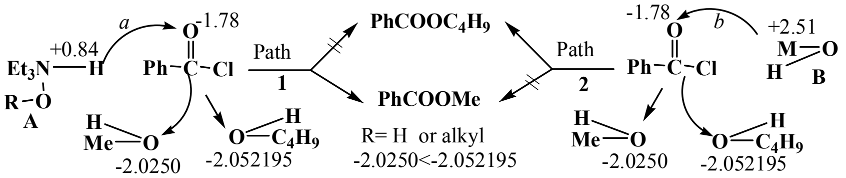


$$\underset{\text{I}}{\mathrm{Ph}\overset{\overset{\displaystyle O}{||}}{C}-\mathrm{Cl}} + \underset{\text{II}}{R-O-H} + \underset{\text{III}}{R'-O-H} \xrightarrow[\text{MeOH}^*]{\text{NEt}_3} \underset{\text{IV}}{\mathrm{Ph}-\overset{\overset{\displaystyle O}{||}}{C}-\mathrm{OR}} + \underset{\text{V}}{\mathrm{Ph}-\overset{\overset{\displaystyle O}{||}}{C}-\mathrm{OR}'},$$

where MeOH = NaOH or KOH. Scheme 2.

The experimental verification of this claim was done in a competitive reaction between benzoyl chloride (I) and different pairs of alcohols (II and III), which are happening in a basic solution (see Sch. 2). The regular correspondence between the estimated amount of donor force of oxygen in alcohols and the direction of the transformation can be found while taking into account one more circumstance of the theory [7, 8]. That's the chemoselectivity of the reaction, which depends on the amount of affinity of the inductive atom of the reagent, which can only be the positively charged atom of the reagent or of the catalyst.

Applying to inductive atoms of bases this means that in aqua complex of triethylamine A the atoms of hydrogen in the bond N–H or O–H can play this role, while in bases B (such as hydroxides of sodium or potassium) metals can do that, as it is shown in the example of methanol and butanol in Sch. 3. The essence is in the fact that the interaction between the reagent (the catalyst in this case) and the substrate does not bring to the hydrolysis of the bond C-nucleofuge of the substrate, but to the partial neutralization of the charge of nucleofuge (the atom with the largest partial negative charge) in this bond and emancipation of the positive charge of its conterion is the electrofuge. Applying to the chlorocarbonyl group of benzoyl chloride means that the real nucleofuge should not be the atom of chloride in the bond C–Cl, but oxygen in the bond C=O. Correspondingly, the inductor of the reaction becomes one of the positively charged atoms of the catalyst, which influences the neutralization of the negative charge of carbonyl oxygen (nucleofuge) and emancipation of the positive charge of its carbon. Next, if this emancipated positive charge of carbonyl carbon is small, it is connected to oxygen of alcohol with a smaller donor force (Sch. 3, Path 1), while if it is large carbonyl carbon connects to oxygen of alcohol with a larger donor force (Sch. 3, Path 2).



Scheme 3. Dependence between the values of charge chemoselectivity of the reaction.

Where R = H, alkyl; Me = Na, K; $AC(H)_{N–H}$ =+0.84, $AC(H)_{O–H}$ =+1.24, $AC(Na)_{NaOH}$ =+2.51 and $AC(H)_{KOH}$= +2.62; –1.78; –2.0250; –2.052195 (u.i.c.) are donor characteristics of carbonyl group oxygen, methanol and buthanol.

It follows from here that since in the complex of triethylamine with water (A, R=H) or with alcohols (B, R=alkyl) a Pauling acid with smaller acceptor force (+1.24 or +0.84 u.i.c.) than the atoms of Na (+2.51 u.i.c.) or K (+2.62 u.i.c.) in the bases B is born, then the chemoselectivity of transformation will correspond to the forces of affinity. Analysis of Sch. 3 shows, that the expected connections between the estimated sizes of donor forces of oxygen in alcohols and chemoselectivity of their transformation into benzoates IV and V can indeed be discerned. All in all, under the influence of a weak inductor of a reaction, triethylamine (in its complex A), between the two different alcohols the one of which oxygen, participates in the reaction is almost exclusively the one with smaller electrodonor force.

For example, in the reaction of equimolar mixtures of methanol and butanol with benzoyl chloride (I) together with triethylamine (row 1a, see Table), the main product of transformation (90:10) becomes methyl (IV), and not butyl ether of benzoic acid (V). A similar chemoselectivity of molecules (II) and (III) can be determined from the difference of donor forces of oxygen from alcohols, which are equal to –2.025 and –2.052195 u.i.c. respectively. For that reason, the preferred formation of the ether with smaller donor force of oxygen is shown in reactions with other pairs of alcohols as well (rows 2a, 3a, 4a, 6a). In other words, in this kind of conditions the main molecules that participate in the reaction are the ones, where oxygen from hydroxy group has a smaller donor force.

Alcohol ROH, II (DF(O))	Alcohol R'OH, III (DF(O))	Ratio of IV:V on the basis of integrals of the protons on PMR		General yield, %
in units of ionic characteristics, u.i.c.		IV:V, %	by unique char. of the group	
1a. CH_3OH (-2.0250)	C_4H_9OH (–2.052195)	90:10	3.88 s (3H, OCH_3); 1.02 t (3H, CH_3, *J* 7.1 *Hz*)	62.5
1b. CH_3OH (–2.0250)	C_4H_9OH (–2.052195)[1]	20:80		66
2a. C_2H_5OH (–2.0495)	C_4H_9OH (–2.052195)	63:37	1.42 t (3H, CH_3, *J* 7.1 *Hz*); 1.02 t (3H, CH_3, *J* 7.1 *Hz*)	60
2b. C_2H_5OH (–2.0495)	C_4H_9OH (–2.052195)[2]	40:60		84.5
3a. $CH_2{=}CHCH_2OH$ (–2.0518)	n–C_3H_7OH (–2.052265)	70:30	4.78 d (2H, OCH_2, *J* 5.6 *Hz*); 4.23 t (2H, OCH_2, *J* 6.6 *Hz*)	60
4a. C_4H_9OH (–2.052195)	$C_8H_{17}OH$ (–2.0522222195)	70:30	4.23 t (2H, OCH_2, *J* 6.4 *Hz*); 3.42 t (2H, OCH_2, *J* 6.4 *Hz*)	55
4b. C_4H_9OH (–2.052195)	$C_8H_{17}OH$ (–2.0522222195)[2]	50:50		85
5a. C_4H_9OH (–2.052195)	i–C_4H_9OH (–2.0544)	50:50	4.3 t (2H, OCH_2, *J* 6.4 *Hz*); 4.07 d (2H, OCH_2, *J* 6.2 *Hz*)	61
5b. C_4H_9OH (–2.052195)	i–C_4H_9OH (–2.0544)[1]	65:35		78
6a. $C_8H_{17}OH$ (–2.0522222195)	i–C_4H_9OH (–2.0544)	75:25	4.3 t (2H, OCH_2, *J* 6.4 *Hz*); 4.07 d (2H, OCH_2, *J* 6.2 *Hz*)	60
6b. $C_8H_{17}OH$ (–2.0522222195)	i–C_4H_9OH (–2.0544)[1]	76:24		65
6c. $C_8H_{17}OH$ (–2.0522222195)	i–C_4H_9OH (–2.0544)[3]	80:20		65
6d. $C_8H_{17}OH$ (–2.0522222195)	i–C_4H_9OH (–2.0544)[2]	56:44		92
7a. $C_6H_5CH_2OH$ (–2.0547865)	C_4H_9OH (–2.052195)	50:50	5.38 s (2H, OCH_2); 4.3 t (2H, OCH_2, *J* 6.4 *Hz*)	52
7b. $C_6H_5CH_2OH$ (–2.0547865)	C_4H_9OH (–2.052195)[1]	0:100		53

[1] 40% aques solution of NaOH; [2] dry KOH; [3] 40% aques solution of KOH.

The opposite order of getting into the reaction for alcohols can be observed, when sodium or potassium hydroxide is used instead of triethylamine. It is interesting, that for a certain pair of alcohols (1b, 2b) this change happens much easier than for others. In these cases a more effective reagent than sodium (4a and 4b, 5a and 5b, 6a and 6b, 6c) or potassium hydroxide (6d) needs to be used, such as dry potassium hydroxide. For example, if from the mixture of butanol and octanol under triethylamine (row 4a) the main product is butylbenzoate (IV), then only with dry KOH it is possible to increase the share of ether of octanol (IV) (row 4b, share of ether increases from 30 to 50%). Thus, as the theory predicted, since the atoms of sodium and potassium have much higher positive charges (2.51 and 2.62 against 1.24 and 0.84 u.i.c.), they enable the inversion of the attack.

These facts also provide evidence for explaining another issue about the induction effect of alkyl groups. Even though this effect increases in the homologue group that happens not because of the increase in donor force, but the decrease in the share of positive charge on α-carbon that goes to oxygen as a negative charge, boosting the electrodonor force of the hydroxy group.

To summarize, these phenomena that we described for alcohols are also seen in amines and similar molecules, and will be reported separately.

Experimental Part. MRI were taken on Mercury 300-Varian with frequency 300 *MHz* in the solution of DMSO–CCl_4, internal standard was TMS.

Synthesis of Ethers IV and V in the Presence of Triethylamine. In a four-necked flask equipped with a mechanical stirrer, dropping funnel, thermometer, and a reflux condenser, 0.025 *mol* of each alcohol and 15 *mL* benzene were placed; 5 *g* (0.025 *mol*) triethylamine was slowly dropped while slowly mixing the solution at 25°*C*. The reaction mixture was cooled to –5–0°*C* and 3.5 *g* (0.025 *mol*) benzoyl chloride was dropped over 15 *min*. Then the temperature was raised to 25°*C* and stirred for another 4 *h*, leaving it to stand until the next day. Water was added until precipitated salts were completely dissolved, the organic layer was separated, and the aqueous layer was extracted with the benzene (3×10 *mL*). The benzole extracts were combined and washed with water. After removing the solvent the residue was distilled, taking out the benzoate fraction without dividing it into components. The yields and PMR data of the outputs are given in Table.

Synthesis of Ethers IV and V in the Presence of Sodium and Potassium Hydroxide. The reaction and its treatment were similar, with the only difference being the use of 2.8 *g* 40% solution of NaOH or KOH instead of triethylamine. The removal of precipitates was done more scrupulously. Overall yield of ethers reached 60–92%.

Received 24.08.2016

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