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ON THE IMPORTANCE OF CHARGE ALTERNATION

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Abstract - The concept of stabilization of polyanionic and polycationic compounds by charge alternation was introduced to explain the course of polymetalation of hydrocarbons and enolates. This concept is generalized to the positional stabilization of polar compounds containing two or more donor or acceptor groups and reconciled with the different known stabilizations of compounds containing a donor and an acceptor group. Various properties of other classes of compounds such as relative acidities and basicities of heterocyclic compounds, charge distribution in cyanines, mesocyanines, oxonoles and aromatic dianions, as well as the regioselectivity of some reactions seem also to obey the rules based on this concept.

The concept of a partial charge appearing on every alternate atom of a conjugated unsaturated system, having one donor or acceptor substituent, is widely accepted and used in chemistry. It is taught and represented by "electron pushing" or by writing resonance structures. Moreover, calculations[1] have shown that in addition to the effect of spreading of the main charge on starred atoms of an unsaturated system, a smaller charge of opposite sign appears on the unstarred atoms leading to an alternation of positive and negative charges. This has been ascribed to π-inductive effects[2], or to polarization, without net charge transfer to or from the multiple bond as discussed by Hoffmann[3]. It was even found by calculation[4] that the inductive effect imposes in saturated systems a charge alternation in contradiction to the previously accepted view that the inductive effect transmitted from atom to atom is always of the same sign, but with rapidly decaying intensity. The charge alternation in saturated systems was challenged[5] by experimental data, but this is now of no consequence since in these systems the field effect is much stronger and this one falls off with the distance.

The alternation of charge was found in a SCF calculation much earlier in the allylic anion.[6] This was assumed to be a contribution to the stabilization of the anion[6,7].

There are systems where resonance justification of alternating charges is not straightforward because of additional effects that are playing a role or because the systems are not alternant, or not planar. We have done work on this kind of system. Some of our results and conclusions have been summarized[8,9]. They were addressed to a rather narrow group of experts working on polylithiation. We want now to present our views on charge alternation, and their extensions to additional fields to a more general public. We would like to show that it is a useful and simple concept, that can predict stabilities and charge distributions in compounds and that its validity can be generalized for additional problem solving. We think that this concept is a very powerful one, since it corresponds to a powerful real effect.

In our work on the metalation of acetylenic fatty acids we have found that dimetalation took place and the second proton was abstracted from the same position as the first one[10] and not from the other propargylic position (1). This was for us an unexpected result, since we assumed that the

$$\begin{tikzcd}
\mathrm{RCH_2C{\equiv}CCH_2R'} \arrow[r, "\mathrm{BuLi}"] & {[\mathrm{RC\overset{*}{H}C{\equiv}\overset{*}{C}CH_2R'}]^-\mathrm{Li}^+} \arrow[d] & + & {[\mathrm{RCH_2\overset{*}{C}{\equiv}CC\overset{*}{H}R'}]^-\mathrm{Li}^+} \arrow[d] \arrow[r] & {[\mathrm{RC\tilde{H}C{\equiv}C\tilde{C}HR}]\mathrm{2Li}^+} \\
 & {[\mathrm{R\overset{*}{C}\text{-}C{\equiv}\overset{*}{C}CH_2R'}]^{2-}\mathrm{2Li}} & & {[\mathrm{RCH_2\overset{*}{C}{\equiv}C\overset{*}{C}R'}]^{2-}\mathrm{2Li}^+} &
\end{tikzcd} \tag{1}$$

second proton would not be abstracted from a site already carrying a charge, but from the other propargylic position leading to a delocalized system spreading out on four atoms with smaller charges on each of them. Instead of this, a system was formed that was less delocalized and contained higher charges on the atoms. Such a polymetalation could proceed to the trilithiated product[11], where all the protons have been abstracted from the same methyl although a second equivalent methyl was present in the starting material (2). The second step of metalation was

$$\mathrm{CH_3C{\equiv}C\text{-}C{\equiv}CCH_3} \xrightarrow{\mathrm{BuLi}} [\mathrm{CH_3\overset{*}{C}{\equiv}C\overset{*}{C}{\equiv}C\overset{*}{C}H}]^{2-}\mathrm{2Li}^+ + [\mathrm{CH_3\overset{*}{C}{\equiv}C\text{-}\overset{*}{C}{\equiv}C\overset{*}{C}}]^{3-}\mathrm{3Li}^+ \tag{2}$$

sometimes faster than the first one (2)(3). These unusual results were explained then by the

$$[\mathrm{PhC{\equiv}CCH_3} + \mathrm{2BuLi} \longrightarrow [\mathrm{Ph\overset{*}{C}{\equiv}C\overset{*}{C}H}]\mathrm{2Li} + \mathrm{PhC{\equiv}CCH_3} \tag{3}$$

spécial stability of the acetylenes dimetalated at one propargylic position (4), that we called then sesquiacetylenes or extended acetylenes[13].

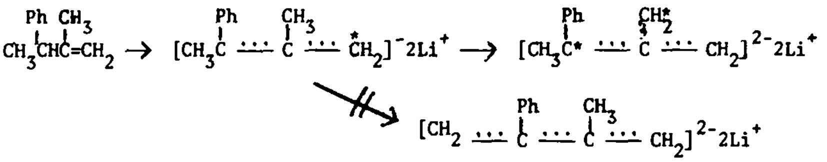
$$[\mathrm{RC} \mathrel{\overset{\cdot\cdot\cdot}{\underset{\cdot\cdot\cdot}{-}}} \mathrm{C} \mathrel{\overset{\cdot\cdot\cdot}{\underset{\cdot\cdot\cdot}{-}}} \mathrm{CR}]^{2-}\mathrm{2Li}^+ \tag{4}$$

Our NMR study carried out on dilithiated acetylenes (5) containing conjugated double bonds to follow the course of metalation by proton resonance has revealed[13,14] a shift of the proton at the 4 position to a field below the aromatic protons indicating a development of a positive charge on

$$\mathrm{Ph\overset{\overset{1}{*}}{C}{\equiv}\overset{2}{C}\overset{\overset{3}{*}}{C}H_2\overset{4}{C}H{=}\overset{\overset{5}{*}}{C}HR} \longrightarrow [\mathrm{Ph\overset{*}{C}{\equiv}C\overset{*}{C}CH{=}\overset{*}{C}HR}]^{2-}\mathrm{2Li}^+ \tag{5}$$

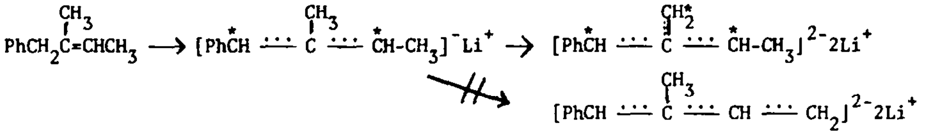
the carbon located between two negatively charged carbons 3 and 5,

Stabilization of charge alternating systems was also found in an additional class of compounds, olefins polylithiated at allylic positions. Here again the question arose whether such a polymetalation is possible and, if it is, from which of these positions the second proton will be extracted, when more than one possibility is available. The results have shown (6) that crossed conjugation was preferred[15] to an extended one. This was also the case when the phenyl could have been incorporated into the extended conjugation (7). The compound (8) with extended conjugation including the phenyl was not obtained.



$$CH_3\overset{Ph}{\overset{|}{C}}H\overset{CH_3}{\overset{|}{C}}{=}CH_2 \rightarrow [CH_3\overset{Ph}{\overset{|}{C}} \cdots \overset{CH_3}{\overset{|}{C}} \cdots \overset{*}{C}H_2]^-2Li^+ \rightarrow [CH_3\overset{Ph}{\overset{|}{C}}* \cdots \overset{\overset{*}{C}H_2}{\overset{|}{C}} \cdots CH_2]^{2-}2Li^+$$

$$\not\searrow\ [CH_2 \cdots \overset{Ph}{\overset{|}{C}} \cdots \overset{CH_3}{\overset{|}{C}} \cdots CH_2]^{2-}2Li^+ \qquad (6)$$



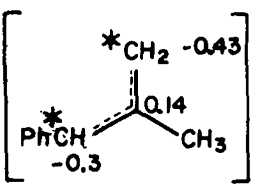
$$PhCH_2\overset{CH_3}{\overset{|}{C}}{=}CHCH_3 \longrightarrow [Ph\overset{*}{C}H \cdots \overset{CH_3}{\overset{|}{C}} \cdots \overset{*}{C}H\text{-}CH_3]^-Li^+ \rightarrow [Ph\overset{*}{C}H \cdots \overset{\overset{*}{C}H_2}{\overset{|}{C}} \cdots \overset{*}{C}H\text{-}CH_3]^{2-}2Li^+ \qquad (7)$$

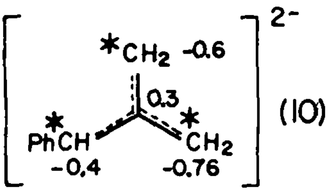
$$\not\searrow\ [PhCH \cdots \overset{CH_3}{\overset{|}{C}} \cdots CH \cdots CH_2]^{2-}2Li^+ \qquad (8)$$

Cross conjugation is generally disfavored relatively to the extended one and one considers that it does not contribute to the stability of compounds.

CNDO/2 calculations that we have performed[15], showed that the net electronic population on the central carbon to which the two or three negatively charged carbons of the mono- and di-anion are linked is positive (9), (10). Moreover they indicated that the phenyl does not contribute more to

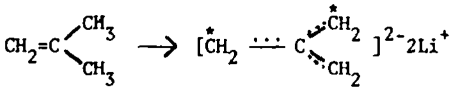
(9)





(10)

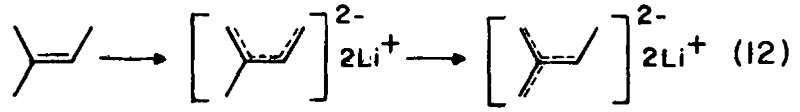
the delocalization of the charge of the dianion than in the monoanion. This observation led us to the preparation of a dilithium compound not stabilized by a phenyl. Metalation of 2-methylpropene with butyllithium in hexane in the presence of TMEDA (tetramethylethylenediamine) led directly[16] to the dilithium derivative of the trimethylenemethane dianion (11), without being able to be stopped at the stage of 2-methylallyllithium. Here again it was found by CNDO/2 calculations[15,17]



$$CH_2{=}C\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix} \longrightarrow [\overset{*}{C}H_2 \cdots C\begin{smallmatrix}\cdots\overset{*}{C}H_2\\ \cdots\overset{*}{C}H_2\end{smallmatrix}]^{2-}2Li^+ \qquad (11)$$

that the most stable dianion species is the planar one and that the central carbon in it is positively charged, with the negative charge distributed evenly on the three methylene groups. A concurrent calculation on the trimethylenemethane dication showed a slightly negative charge on the central carbon.

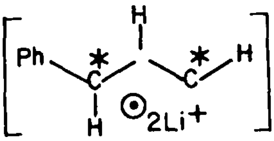
The dilithium salt of the trimethylenemethane dianion was stable and could be preserved even at room temperature. The dipotassium salt of trimethylenemethane dianion was also prepared from 2-methylpropene. Although the isomeric butadiene dianion was prepared by Bates[18], it was shown[19] that the cross-conjugated dianion was more stable than the extended one (12).



(12)

Further metalation of allylithium was also studied to determine the position of metalation. The second proton was abstracted from the terminal position, already carrying a charge. This metalation being slow, we metalated phenallyllithium and again the proton was abstracted from the terminal position already carrying a charge[20] to give the dilithium derivative (13). The structure of this compound was calculated independently by Streitwieser[21] and Schleyer[22].

The greater stability of the cross vs. extended conjugated compounds was attributed initially to the Y-aromaticity, as proposed by Gund[23]. However, the negative overlap between the methylenes of the dilithium trimethylenemethane and the fact that the barrier to rotation[17] in the homologous 10π-electron compound (14) was not higher than in allylic or pentadienylic lithium compounds led us to doubt this hypothesis. We tested this concept on an analogous class of compounds, at that time unknown, the dilithium salts of xylylene dianions. Indeed, the xylenes did undergo dimetalation[2] at the benzylic positions (15) and the most easily metalated one was the meta isomer, then the ortho and finally the para isomer that preferred gem-metalation. p-Xylene was however di- tri- and tetra-metalated at both methyls by butylpotassium[25].



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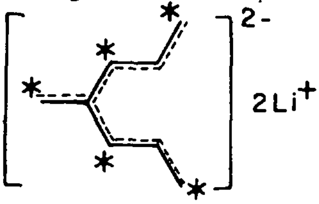

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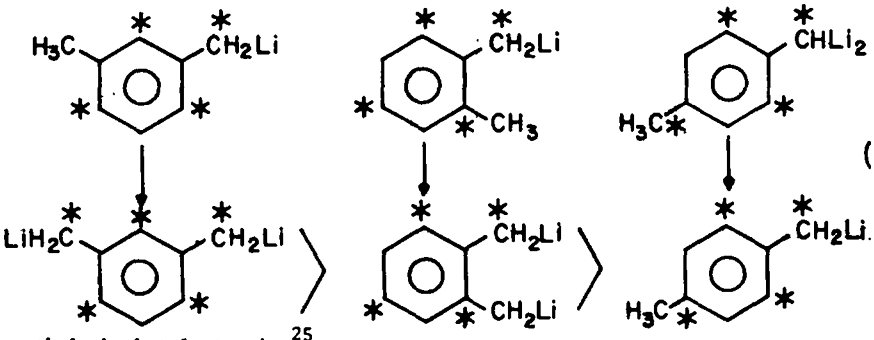
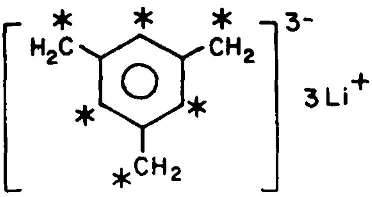


(15)

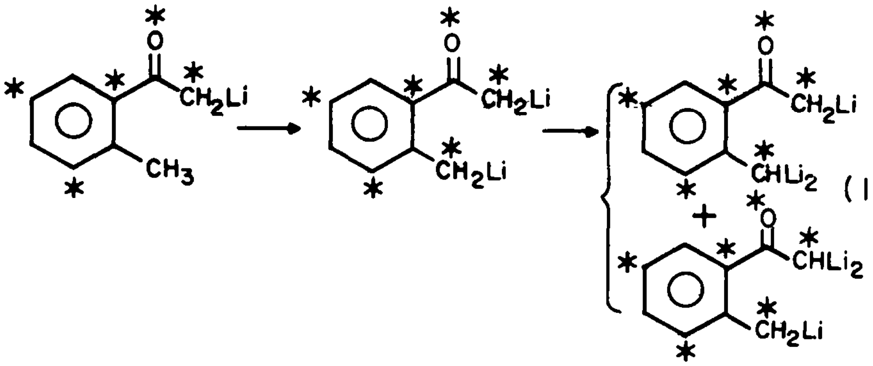
In order to pronounce a compound aromatic or not, one has to define the concept of aromaticity. Unfortunately, there is a great amount of confusion in this respect. Some scientists confound aromaticity with stbailization. Evidently, aromaticity is some special manner of stabilization. We referred to two additional criteria generally used by organic chemists, i.e. cyclic delocalization and (4n+2)π electrons in the system. It is evident that no cyclic delocalization involving the two methylenes can take place in the dianion of m-xylylene, the most stable of the three isomers. Moreover the number of electrons in the system has no bearing on the stability of these systems as evidenced by the trimetalation[25] of mesitylene, that leads to a 12 electron π-system (16). This metalation was as facile as that of m-xylene. The tripotassium salt of this compound was obtained by metalation with butyllithium/potassium t-butoxide, showing that it is not the cation that determines the course of metalation.



(16)

The two criteria point therefore against the inclusion of these compounds into the class of aromatics. There must be therefore some other drive for their stabilization.

Metalation of enolates of acetophenones[26] having methyl groups on the ring gave some additional insight into this problem. In this case there were the ortho and para methyls that were metalated but not the meta, in apparent contradiction with the course of metalation of the xylenes. Moreover, some additional metalation at the α-position to the carbonyl group took place. These were the first reported gem α,α-dimetalated ketones (17).


(17)

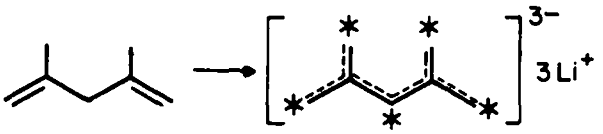
We also addressed the problem why is it possible to get lithium derivatives starting with a derivative of a monoanion, butyllithium. CNDO/2 calculations[24] have indeed shown that the dianions of xylylenes are far less stable than those of benzyl, but their lithium derivatives are of similar stability. Interaction of a dianion with two lithium cations adds considerably to the stability of these products.

All the monometalations proceeded in a normal manner, that could be predicted by the usual considerations. The course of the second and further steps of metalation yielded results often unexpected. This is a very general problem of the effect of a group already in the molecule on the relative stability of additional groups in various positions of this molecule. This problem has been addressed very rarely. A review[27] containing calculations of energies of polysubstituted benzenes has been published, but its conclusions cannot be generalized to other classes of compounds. In our case, the groups (the charged methylenes) interact strongly with the rest of the molecule and therefore their preference for particular isomers is pronounced.

The general rule for polymetalations[7] of conjugated systems is, that it will take place in such a manner as to introduce the negative charge on the atoms that already carry such a charge. In other words, if we have a charged unsaturated system containing methyl substituents where the charge is located on the starred set of atoms, as the case is in conjugated monoanions, the methyl that will be metalated is the one that is starred also (linked to an unstarred position). This will lead to an expansion of the delocalized system by one atom. If no such methyl is present in the molecule, then the metalation is preferred at a geminal position. This however is not always the case, because of larger charge repulsions and since no extension of the delocalized system takes place.

The reason for this course of the metalation is that in this way charge alternation is maintained[7] in the molecule and charge alternation has a strong stabilizing effect.

Examples for this rule are equations (1), (2), (3), (5), (6), (7), (8), (9), (10), (11), (12), (13), (14), (15), (16), (17). Two additional examples can be invoked. Bates has prepared the trilithiated compound[18] from 2,4-dimethyl-1,3-pentadiene (18) but 3-methyl-1,4-pentadiene yielded only the monolithiated[18] product (19) since the methyl was unstarred.



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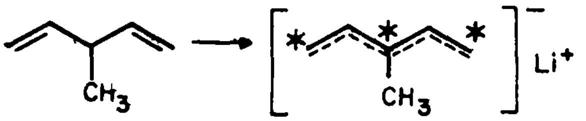
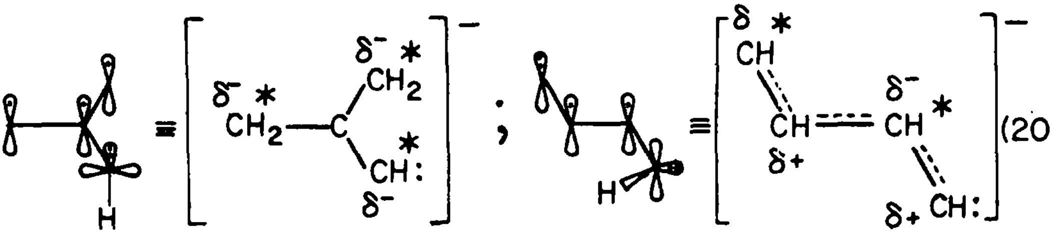


(19)

The idea of the aromaticity of trimethylenemethane dianion was invoked recently again by Agranat and Skancke[28] and particularly by Inagaki[29]. Inagaki applied his criteria for continuity-discontinuity of cyclic conjugation[30]. However his definition of cyclic conjugation involves configurations and does not mean in this case direct cyclic conjugation between the methylenes through space. It seems that the definition of Inagaki involving charge transfer and excitation configurations leads to charge alternation. This can be seen in another example for the continuity of cyclic conjugation discussed by Inagaki[31]. The crossed anion of allylcarbene prefers the perpendicular conformation, whereas the extended isomer - the planar conformation (20), where the vacant p orbital is conjugated with the allyl anion and that means charge alternation.

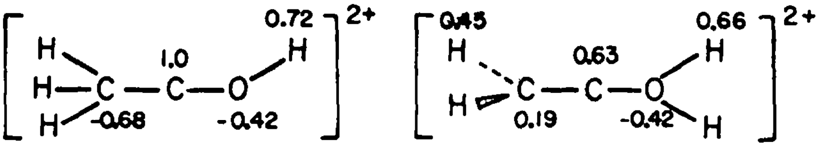


(20)

All that was said before on polyanions (more exactly: polylithium or potassium compounds) applies also to polycations. An analogous charge alternation is expected to occur there. These compounds, however, are generally unstable in solution. They are formed in the gas phase and some of them have been calculated by Schwarz[32] (21). However a number of extensively delocalized dications have been observed in solution[33,35] and particularly a derivative of trimethylenemethane dication with pronounced charge alternation[36] (22). This is not due to Y-aromaticity since a linear dication[37] with a bridging electronegative atom was prepared (23). In such arrangement the charge alternation contributes to the stabilization of the dication.

Some additional results of calculations of anions and cations[38,39], carried out by ab initio methods are shown in (24) - (26).

Schleyer's group[40,41] has determined the charge distributions (27) by ^{13}C NMR and by MNDO calculations (numbers in parenthesis). Additional calculations by this group[40,41] have shown that the trimethylenemethane dianions with cross-conjugation, showing charge alternation are more stable than



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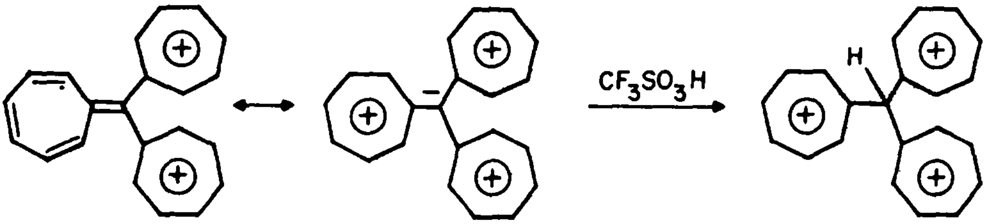

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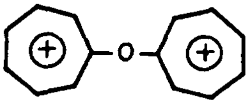

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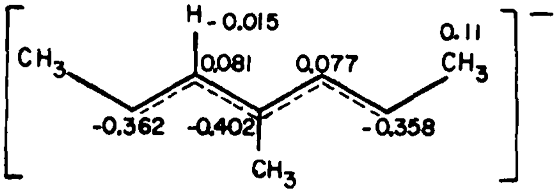

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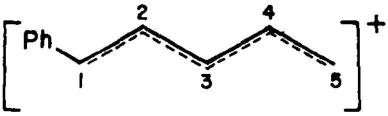
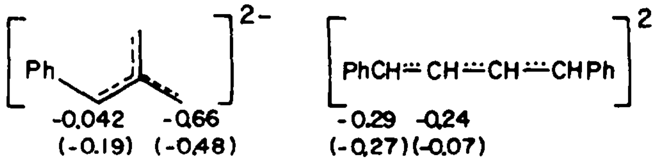


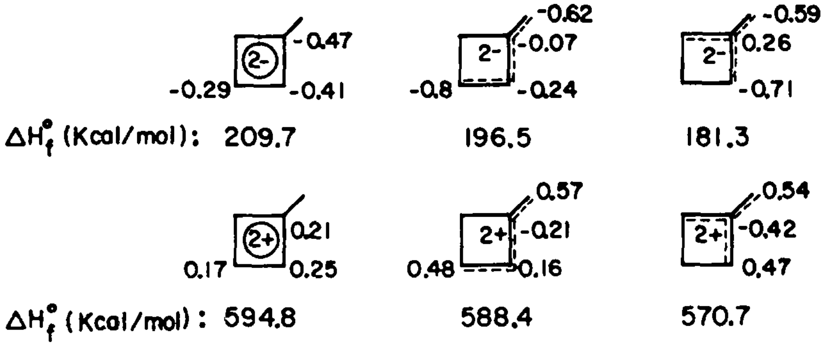
	C(1)	C(2)	C(3)	C(4)	C(5)
Total charges	0.246	-0.059	0.239	-0.013	0.135
P_z charges	0.346	-0.087	0.312	-0.044	0.209

(25)



(26)

than extended isomers or even of isomeric aromatic systems of cyclobutadiene dication and dianion. The calculated (MNDO) charge distribution[41] in isomeric dicationic and dianionic aromatic compounds and isomeric compounds with extended and cross-conjugation, as well as their heats of formation[40,41] are shown (27). The charge alternating cross-conjugated compounds have been found to be more stable than the uniformly charged aromatic isomers. A recent calculation of cyclobutadiene dianions showed that it is not planar and contains two long and two short bonds. It is composed of an allylic anion and a localised charge.



(27)

The charge alternation does not always impose cross-conjugation. Indeed extended charge-alternating systems are the majority. The cross-conjugated systems have focused attention on the charge alternation because they have been unexpectedly more stable than their extended isomers.

The reason for the stability of the charge alternating systems seems to be the presence of a large number of polar bonds. The alternating atoms with partly positive and partly negative charges represent an alternation of donor and acceptor sites. Indeed such an alternation is not limited to ions. It applies to any compound having more than one donor or acceptor group. We have formulated[9] earlier our conclusions concerning such systems in a number of rules:

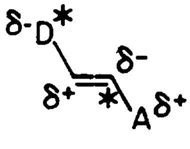
(1) Highest stabilization of a conjugated system is achieved when the number of donor-acceptor interactions is the largest possible. This takes place with alternating partial charges on neighboring atoms.

(2) Two or more substituents of the same kind (donors or acceptors) are the most stabilizing when they are placed all on the starred atoms of the system.

(3) Two substituents of different kind are stabilizing when one is located on a starred and the other on an unstarred atom of the set.

These rules resolved the apparent contradiction between our findings that our cross-conjugated systems were more stabilized than the extended ones and the usually accepted view that the opposite is correct. Indeed, the interactions that were generally considered were of systems containing a donor and an acceptor. In these cases, the extended conjugation with the donor on a starred and the acceptor on an unstarred atom will be the most stabilized, since this is the positioning that leads to charge alternation (28). The rules permit to predict the stability of olefins and aromatic compounds with more than one substituent (29).

Already Pauling[43] has correlated bond energies with electrostatic effects in polar bonds. A number of research groups[44-46] have recently extended this electrostatic approach to bonds that were considered non-polar or weakly polar to explain the relative stabilities of isomers and their properties. In our concept we try to look not only on the separate bonds but on the whole system, since we believe that polarization is transmitted not only to the next atom, but further, and the polarization from different groups acting in the same manner is the most stabilizing. This kind of polarization, leading to charge alternation is not accompanied by



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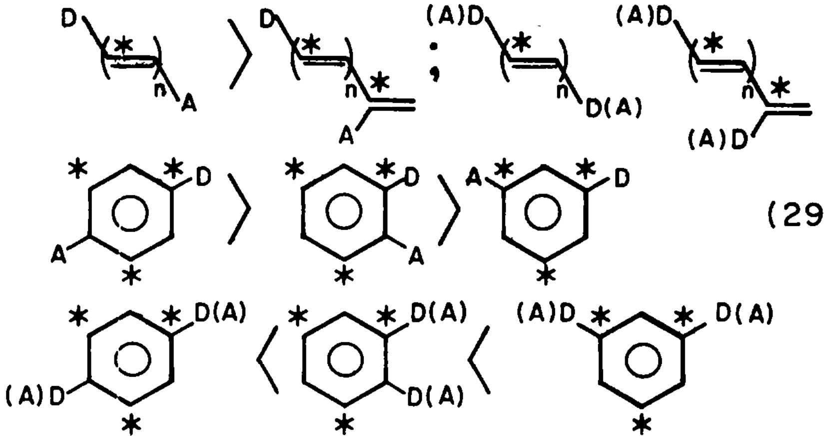


(29)

large dipole moments and hence does not suffer from the destabilizing effect of large dipole moments created in systems with end-to-end polarization consisting of a gradual change of the magnitude and not the sign of the charge from atom to atom.

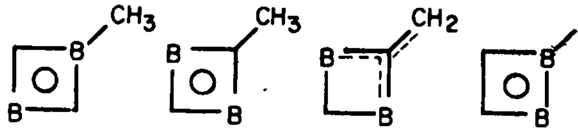
A good example for the effect of combined polarization was given by Benson[44] (30). Calculations show that the hypothetical reaction (30) is attended by release of 12 kcal/mol, and, although the number of C-H and C-F bonds remains the same the molecules having more than

$$2CH_3F \rightleftarrows CH_4 + CH_2F_2 + 12\ \text{kcal/mol} \qquad (30)$$

one substituent of the same kind are preferred. This is too strong an effect to be of anomeric[47] origin. (The difference in energy between 1,3- and 1,4-dioxane is only 8 kcal/mol). Moreover, the anomeric effect can be considered as a mechanism by which charge alternation takes place. Benson has treated the general problem of disproportionation: $2XAB \rightleftarrows XA_2 + XB_2$ and reached the conclusion, that when the partial charges on A and B have the same sign then this disproportionation is favored. Two donors and two acceptors on the same atom, even in a saturated system, are therefore always preferred to a donor and acceptor on the same atom.

A similar situation prevails in unsaturated systems. 1,1-difluoroethene is by 6 kcal/mol more stable than the other isomers of this compound. A polarization took place, leading (we assume) to a partly positive charge on the carbon to which the two fluorines are linked and a partly negative one on the other carbon. This leads to a weakening of the C-C bond, as evidenced by the π-dissociation energy[48] in $CH_2{=}CF_2$ (62.1 kcal/mol) relative to the energy in $CH_2{=}CH_2$ (59 kcal/mol) and $CF_2{=}CF_2$ (52.5 kcal/mol). It is not the presence of the fluorine substituents that makes the bond stronger but their gem substitution on one carbon that influences not only the strengths of the C-F bonds themselves, but the C=C bond also by inducing its polarization.

Additional examples of the stabilization of neutral compound exhibiting evident charge alternation can be found in some calculations carried out in Schleyer's laboratory[40,41]. The standard heats of formation of most stable isomeric compounds containing two boron atoms and a four-membered ring are shown (31). The least stable compound contains two neighboring boron atoms. No charge alternation is possible in this case. The most stable isomer is an aromatic one containing the boron atoms at the 1 and 3 position in the ring. A less stable aromatic isomer contains the boron atoms at the 2 and 4 positions. In both these compounds there is evidently induced charge alternation that stabilizes the aromatic ring. The non-aromatic cross conjugated isomer containing the two boron atoms at the 2 and 4 positions is more stable than its aromatic counterpart having a similar arrangement of the boron atoms.



(31)

ΔH_f° (Kcal/mol) 15.0 20.7 18.9 27.6

Polarization of an aromatic compound to a charge alternating system leads to stabilization. One could therefore expect that perturbation of an aromatic compound, e.g. by replacing a carbon with a nitrogen atom, will lead to charge alternation and that the introduction of an additional substituent will be favored at positions where this charge alternation will be increased. This indeed can be seen from the results of calculation of Del Bene[49] (Table 1).

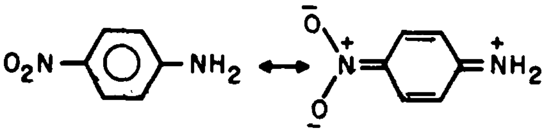
Mulliken Population Data of 4-Substituted Pyridines R-

R	N_1	$C_2;C_6$	$C_3;C_5$	C_4	Total densities	
					N	ring
H	1.048	0.988	1.004	0.967	7.241	41.075
NH_2	1.105	0.965	1.091	0.915	7.268	40.977
CH	1.084	0.967	1.076	0.997	7.255	40.935
F	1.069	0.973	1.042	0.967	7.246	40.876
CHO	1.039	0.989	0.997	0.979	7.233	40.991
CN	1.028	0.986	0.983	1.021	7.224	40.891

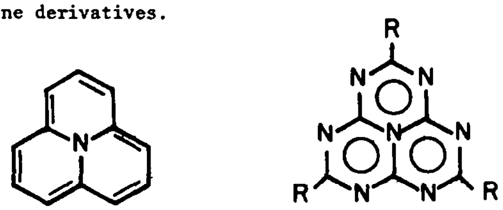
J.E. Del Bene, J. Amer. Chem. Soc. 101, 6184 (1979).

The parent pyridine ring is polarized, having an excess of π-electron density at the nitrogen and the 3 and 5 carbons. Introduction of a donor at the 4 position, where the compound is more stabilized than with the same donor at the 3 position, increases the difference of charges between the neighboring atoms. The charge is not transferred to the nitrogen in the ring, as generally explained in chemistry classes, but mainly to the 3 and 5 positions. At the same time the 2 and 4 positions are depleted of electron density. On the other hand, introduction of an electron receptor at the 4 position, where it is known to be less stabilizing than at the 3 position, causes a diminishing of the charge differences between the neighboring atoms.

A similar conclusion could be reached from the calculations[50] carried out on p-nitroaniline and p-nitrophenol. It appeared that the usual explanation of the stabilization of these compounds by charge transfer from the amino to the nitro group (32) is not correct. Chrage is transferred from the amino group to the ring but not to the nitro group.


(32)

Stabilization takes place also when similar atoms are introduced into the aromatic ring at odd positions to each other. Thus the unstable tricyclic biradicaloid cycl[3.3.3]azine is stabilized[51] when other nitrogens are introduced at the appropriate positions in the ring (33) give fireproof materials, of cyamelurine derivatives.


(33)

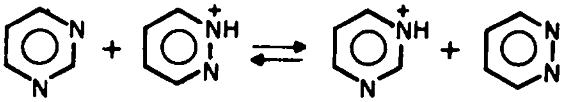
The charge alternation in heterocyclic amines can be deduced from the ^{13}C NMR shifts of pyridine, pyrimidine and pyridazine[52].

The interaction of two substituents with an aromatic ring was discussed recently[27,53,54]. Anilines containing donors at the meta are more stable than at para position[53]. The opposite happens with anilinium salts. Aniline is stabilized by acceptors more when at the 4- than at the 3-position. Pyridines are stabilized by donors at the 4-position and by acceptors at the 3-position. Results similar to those for aniline have been found for phenols and fluorobenzenes and opposite stabilizing effects for benzonitriles[27]. The results correspond in general to (28) and to the principle of stabilization by charge alternation.

It is interesting that calculations show 1,3-difluorobenzene to be more stable than its 1,4-isomer[27] despite its dipole moment and the absence of it in the 1,4-isomer. The π-charge transfer from the donor to the ring is not diminished and sometimes increases after the introduction of n-other donor at the 3-position, but it is diminished for the 1,4-isomer.

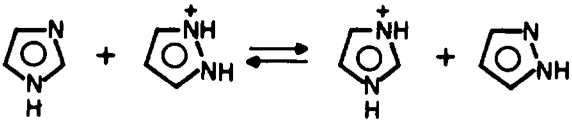
The stabilization of benzenes with similar substituents at meta positions makes these compounds more refractory than their isomers to electrochemical oxidation and reduction[55]. Electron affinities[56], determined by measuring equilibrium constants for gas-phase electron-transfer reaction with a pulsed ICR mass spectrometer, show that benzenes having two acceptors in the meta have a lower electron affinity than their para isomers. The opposite shows up when a donor and an acceptor are on the ring.

Many differences in acidity and basicity of isomers can be explained in terms of charge alternation. The smaller gas-phase basicity[57] of pyridimine than of pyridazine (34) and in contrast, the larger basicity[58] of imidazole than that of pyrazole (35) and in addition, the smaller gas phase basicity of the conjugate base of imidazole than that of the conjugate of pyrazole (36) can all be attributed to the stabilization of the less basic and less acidic isomers by charge alternation. When two atoms of the same character, either basic or acidic, are at 1,3 positions to each other they induce at the atom between them a



(34)

ΔG°(g) = 4.6 ± 0.2 Kcal/mol

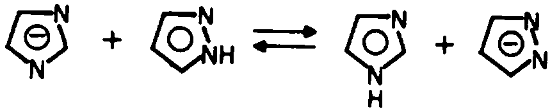


ΔG°(g) = 10.9 ± 0.2 Kcal/mol

(35)

charge of the opoosite sign, thus leading to the stabilization of the system.

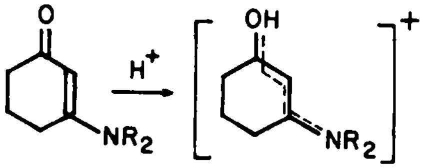
A similar explanation can be given to the unique basicity[59] of the conjugated aminocyclohexenone (37), where it is the oxygen of the carbonyl and not the amine that is protonated. Protonation of the amine would have removed this group from conjugation and diminished the charge alternation. Two donors at odd positions of a delocalized cationic species stabilize



ΔG°(g) = 3.6 ± 0.2 Kcal/mol

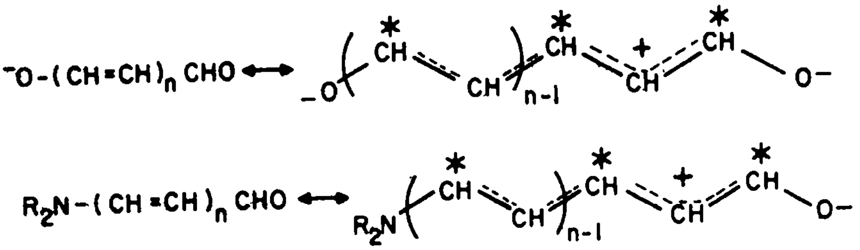
(36)

this species very strongly, according to our second rule. This effect was encountered very early in the cyanine dyes[60], although it was obscured by the resonance forms that had been written for them (38). Indeed, a better representation of them is as an odd carbon-conjugated cation with two donor groups at odd positions (38). This representation can explain



(37)

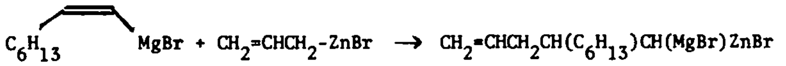
not only the partly positive charges on the odd-numbered carbons, but also the negative charges on the even-numbered ones. It is in these compounds that charge alternation was found for the first time experimentally by NMR and supported by calculations[61-65]. The positively charged carbons react with nucleophiles and the negatively charged ones with electrophiles[64]. Dähne[65] has discussed their properties in terms of a special class of stabilized compounds, the polymethines, as a function of the number of electrons located on the system. It is much simpler and without the need of counting electrons to look at them as described above. Also the other classes of stabilized compounds, the anionic oxonoles and the neutral merocyanines can be seen as double bonds stabilized by a donor and an acceptor (39) located on a starred and unstarred atom respectively, or as a delocalized cation with two donors on starred atoms. This time the substituents are located one on an odd-numbered and the other on an even-numbered atom, according to our third rule.



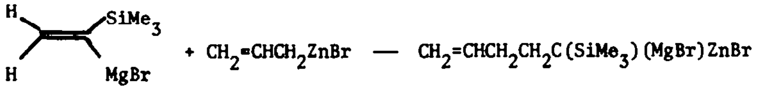
(39)

Stabilization by charge alternation is the reason for the unexplained until now preferential formation of gem vinylic and saturated dimetallic compounds in a series of reactions. Hydroboration[66] (40) and hydroalumination[67] (41) of acetylenes leads to gem diboron and dialuminum compounds respectively. This course of the reaction is not due to the four-center mechanism since the non-catalyzed addition of allylzinc bromides to vinylic magnesium compounds[68] leads to gem dimetallic (42) or even trimetallic products (43). Moreover, carbotitanation of vinylic aluminum compounds[69]

$RC{\equiv}CH + R'_2BH \rightarrow RCH_2CH(BR'_2)_2$ (40) $C_3H_7C{\equiv}CH + R'_2AlH \rightarrow C_3H_7CH_2CH(AlR_2)_2$ (41)



(42)



(43)

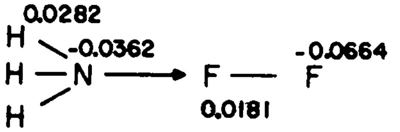
in the presence of trimethylaluminum, a reaction known to give the thermodynamically most stable product, containing the titanium at the unsubstituted end of the chain, gave again the gem dimetallic compound (44). Metalation of a gem dimetallic compound with butyllithium introduces lithium as the third metal on the same carbon[70] (45). In all these products additional negative charges are introduced on a negatively charged carbon α to a metal without much destabilization,

$$C_5H_{11}C{\equiv}CAl(CH_3)_2 + (CH_3)_3Al \xrightarrow{CH_2TiCp_2} C_5H_{11}C(CH_3){=}C[Al(CH_3)_2](TiCp_2) \qquad (44)$$

$$Ph_2AsCH_2Si(CH_3)_3 + BuLi \longrightarrow Ph_2AsCHLiSi(CH_3)_3 \qquad (45)$$

since the larger negative charge interacts with two or three positive metal atoms in the fragment $\overset{\delta+}{M} - \overset{\delta-}{C} - \overset{\delta+}{M}$, where charge alternation takes place.

The stabilization of molecules or aggregates by donor-acceptor interaction and the charge transfer linked to it has been strongly emphasized by Gutman[71]. He has given a number of examples showing charge alternation. Complex formation between ammonia and fluorine[72] is accompanied by changes in electron density on the atoms (46). A transfer of charge takes place from ammonia to



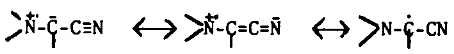
(46)

fluorine, but the electron density is increased on the fluorine away from the nitrogen and decreased on the fluorine next to it. The electron density on nitrogen is increased by taking it from the hydrogens. All this leads to charge alternation. Similar conclusions can be reached from the work of Streitwieser[73]. Abstraction of a proton from the methyl group of dimethyl sulfone makes the

$\bar{C}H_2$-S bond shorter, the S-O and S-CH_3 longer, the oxygen more negative and the sulfur more positive.

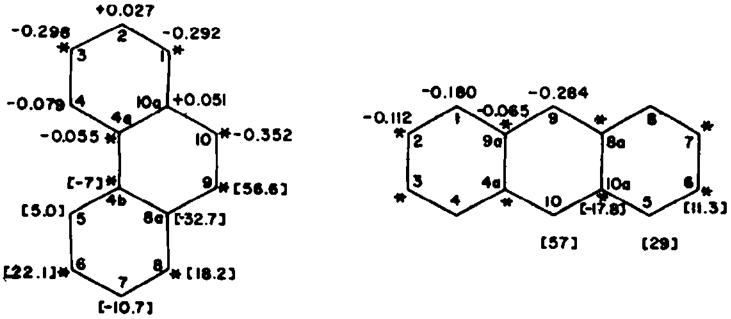
The effect of charge alternation can be found also in transition states. Jorgensen[74] has found in his calculation of the transition state of the attack of hydride on formaldehyde that the carbon was even more positive than in formaldehyde and the hydrogens more negative.

The capto-dative radicals[75] are stabilized by having a donor and an acceptor on the same carbon. This arrangement seems to contradict our third rule. However, this is not contrary to our basic understanding of the stabilization mechanism, since these radicals are the only known species where charge alternation occurs with a donor and an acceptor on the same atom (47). Kosower[76] and Katritzky[77] have emphasized before the charge alternation in these free radicals. However the differential stabilization of the various olefins has also to be taken into account. A self consistent reaction field calculation[78], taking into account solvation energies, revealed a stabilization of radicals substituted by a donor and an acceptor due to charge separation. In the method of evaluating the capto-dative stabilization by the rate or addition of free radicals to appropriate olefins, the eventual stabilization or destabilization of the olefin by the substituents has also to be taken into account, before drawing conclusion on the stabilization of the capto-dative radical. A double bond with a donor and acceptor on the same atom will be destabilized relative to a bond with two donors or two acceptors on the same atom.



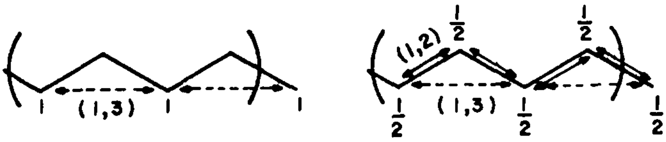
$$>\overset{+\cdot}{N}-\underset{|}{\bar{C}}-C\equiv N \longleftrightarrow >\overset{+\cdot}{N}-\underset{|}{C}=C=\bar{N} \longleftrightarrow >N-\underset{|}{\dot{C}}-CN \qquad (47)$$

Reduction of aromatic or other cyclic unsaturated compounds with metals leads to salts of dianions. Most of these compounds have symmetry properties that make full charge alternation impossible. An axis or a plane of symmetry bisecting a bond requires that the two neighbouring atoms on this bond have the same charge. The driving force towards charge alternation leads then to two systems on both sides of the symmetry element where each of them reveals charge alternation (48). This happens in dianions that are aromatic, non-aromatic or antiaromatic[79], showing that charge alternation is a basic effect common to all these systems. The unbracketed numbers on (48) represent the difference between the calculated (ωβ) charge density of the indicated carbon in the neutral and in the doubly charged system. The bracketed numbers are the respective changes in the ^{13}C chemical shifts.



(48)

The charge distribution in dianions of aromatic compounds depends on the structure of the LUMO and therefore also of the other molecular orbitals. Charge alternation was found to be a general phenomenon and this simple concept can often predict the charges on atoms. One has therefore to assume that these charges are not due to the particular arrangement and form of the molecular orbitals, but these orbitals take a form to give an expression to the donor acceptor alternation. A simple calculation of electrostatic interactions in an extended system or a four-atom fragment of it for the two alternative distributions of two charges between the atoms, one with the charges equally distributed on all of them and the other with the charges located on every alternate atom, shows that the second arrangement is the more favorable. Only 1,2 and 1,3 interactions have been taken into account (49) and the CCC angle of 120° was assumed. The electrostatic interactions



(49)

in the cross-conjugated trimethylenemethane dianion or dication are even more favorable than that of the extended species.

The purpose of this paper is to point out that the donor-acceptor and charge alternation is a real effect and that the principle of donor-acceptor and charge alternation can be applied very extensively. The phenomenon of charge alternation was noted previously in some special systems. We wanted,however, to show that this phenomenon is not just a consequence of an orgbial perturbation, but a way by which a molecule stabilizes itself. This happens not only in the well known case of a donor and acceptor disposed on vicinal positions of double bond or 1,4-positions of an aromatic ring, but even when several donors or several acceptors are appropriately disposed in unsaturated and even in saturated systems. The charge alternation concept is a working principle that can be used to evaluate relative stabilities of compounds. Although qualitative, this concept has the advantage of simplicity, generality, and of a structural and topological approach. A number of scientists[80-8 have pointed out the importance of having a qualitative model and even the supriority of such a model over a mathematical representation.

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