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THEORETICAL CALCULATIONS OF CHEMICAL INTERACTIONS-III

THE REACTION OF HALONITROBENZENES WITH NUCLEOPHILES

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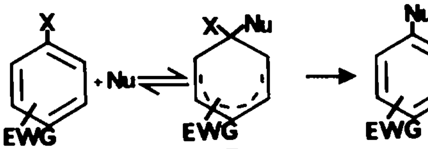
ABSTRACT - Potential σ-zwitterionic complexes formed between fluorobenzene, p- and o-nitrofluorobenzene with ammonia and amide ion where calculated by CNDO, INDO and MNDO semiempirical methods with a wide geometry optimization. Data for bond lengths, bond angles and charge densities are given. In the case of the complexes with ammonia the reaction coordinate was also calculated by the MNDO procedure. The obtained results show that theoretical calculations can provide useful data on these type of complexes and provide models for systems not amenable to experiment yet.

The study of σ complexes Z formed as intermediates in nucleophilic aromatic substitutions (NAS) proceeding by the widely accepted two step mechanism (eq. 1) proposed by Bunnett,[1] has received a considerable interest in the last years,[2] mainly focused in the quantitative determination of the complex stability and its kinetics of formation.[3-8] Because of its mechanistic relevance on most NAS many investigations were formerly devoted to the structural characterization of complexes. When X and Nu are oxygenated groups (eg. OCH_3, OC_2H_5)[9] the complexes are stable enough to allow certain determinations.



Z

(1)

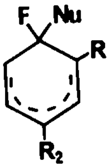
But, when the substrate is poorly activated and specially when the nucleophile is an amine, the complex is so unstable that precludes any experimental measuring.

In cases like this, a MO study of the molecular properties can provide a useful alternative until suitable experimental techniques are developed.[10] To our knowledge only a few MO treatment of σ-complexes like Z have been performed using all valency electron SCF-MO calculations.[11] Most studies were carried out using more simple methods such as: extended Hueckel,[12] Parisser-Parr-Pople,[13] and β-variable.[14] We have previously reported some SCF-MO calculations of substrates and nucleophiles suitable for complex formation.[15] In the present paper we describe a detailed semiempirical SCF-MO study of the σ-complexes derived from the reaction of fluorobenzene, o- and p-fluoronitrobenzene with ammonia and amide ion.

Methods of Calculation. Although the complex formed by fluorobenzene could be calculated by an "ab-initio" method in its simplest level, the nitrosubstituted and other related molecules of interest to this subject exceed the capacity of the available programs and, therefore, "ab-initio" calculations were excluded. The CNDO, INDO[16] and MNDO[17] semiempirical methods are of an approximation level suitable for the purpose of this study since they do not represent a severe simplification of the problem. MNDO has been previously used to reproduce some properties of transient species[18] and organic reactions[19] but it has not been applied before to the study of NAS. The claculations were carried out using programs GEOMO (QCPE 290) and MNDO (QCPE 353) using the optimization algorithms developed by Rinaldi[20a] and Davidson-Fletcher-Powell,[20b,c] respectively. In all cases the original parameters were used. The MNDO QCPE program was modified to allow accomodation of 99 basis atomic orbitals. The population analysis was performed by the Amstrong, Perkins and Stewart's (APS) method.[21] The computation was carried out using an IBM 370 computer located at IBM Argentina.

RESULTS AND DISCUSSION

In the present paper X=F and the complex has the structures shown below



Z1 Nu=NH_2^- ; Z2 Nu=NH_3
a, R_1=R_2=H
b, R_1=NO_2 ; R_2=H
c, R_1=H ; R_2=NO_2

With the aim of keeping computational time within reasonable limits only partial geometry optimization was carried out. Two different criteria were examined: A) to keep C3, C4 and C5, and their substituents coordinates unchanged, or B) to constrain C2-C6 atoms in a plane. In both cases the rest of the geometry was free to optimization.

System A assumes that the complex formation do not modify the remote C3-C5 geometry, while system B takes into account some X-ray data on related complexes.[22]

Attack by Amide Ion. Table 1 gathers some geometry data for complex Z1a obtained following system A, using CNDO, INDO and MNDO methods. It can be observed that CNDO and INDO give similar results, while slight differences are exhibited by the MNDO. The main features are the elongation of C1-F and C1-N bonds with respect to substrate and product bond distances, respectively. Angles at C1 are close to an sp^3 hybridization; this allows the conclusion that Z complexes are real σ complexes. In the 2,4-dinitro-naphtalene series, for X=OCH_3 a transient species of similar structure was detected by the use of high resolution flow nmr.[23] The MNDO is more adequate to reproduce C1 sp^3 angle. The short C2-C3 distances give a 1.6 bond order by the three methods. The charge density shows an alternate ring distribution with the expected C2 and C4 negative charges, the main negative charge being supported by the fluorine atom. When the same calculations were performed for complex Z1a with coplanar C2-C6 atoms, similar results were obtained for bond distances, bond orders and charge densities.

Table 1

Bond lenghts[a] and angles[b] for complex Z1a

Method Bond	CNDO	INDO	MNDO
C1-F[c]	1.390(1.35)	1.404(1.36)	1.385(1.33)
C1-N[d]	1.436(1.39)	1.435(1.39)	1.501(1.42)
C1-C2	1.463	1.458	1.523
C2-C3	1.365	1.371	1.377
C3-C4	1.400	1.400	1.410
C1-plane[e]	0.039	0.050	-0.019
Angle			
F-C1-N	99.3	96.5	106.1
C6-C1-C2	111.2	111.5	112.1

[a] (Å); [b] (°); [c] Values for the substrate between brackets; [d] Values for the product between brackets; [e] Positive towards fluorine.

The effect of substituents is very important on this type of reaction that only occurs at a measurable rate when the ring is activated by electron withdrawing groups. Complexes with an ortho (z1b) and a p-nitro group (Z1c) were calculated by the three methods, the optimized bond distances are shown in Table 2. Compound Z1c has a symmetry axis and, therefore, systems A and B give similar results.

Table 2

Bond lengths[a] and angles[b] for complexes Z1b and Z1c

	Complex Z1b			Complex Z1c		
Method Bond	CNDO	INDO	MNDO	CNDO	INDO	MNDO
C1-F	1.384	1.398	1.372	1.382	1.394	1.377
C1-N	1.426	1.420	1.494	1.427	1.423	1.493
C1-C2	1.473	1.469	1.535	1.467	1.464	1.529
C1-C6	1.469	1.467	1.542	1.467	1.464	1.528
C2-C3	1.402	1.407	1.427	1.350	1.355	1.363
C5-C6	1.347	1.351	1.356	1.351	1.354	1.362
C3-C4	1.368	1.369	1.377	1.420	1.421	1.442
C4-C5	1.419	1.419	1.439	1.420	1.423	1.443
C-NO_2	1.393	1.396	1.437	1.434	1.439	1.436
N-O	1.233	1.234	1.227	1.234	1.236	1.226
N-O'	1.237	1.240	1.225	1.234	1.236	1.226
C1-plane[c]	0.08	0.07	-0.07	0.00	0.02	-0.03
Angle						
F-C1-N	105.9	105.4	108.6	106.0	105.5	107.4
C2-C1-C6	111.2	111.5	111.7	110.5	111.0	111.4
NO_2-pl.	3.7	7.4	1.1	0.1	0.6	0.3

[a] (Å); [b] (°); [c] Positive towards fluorine.

Comparison with complex Z1a shows shorter C1-F and C1-N distances suggesting a more stable compound, as is shown by the increased bond order close to 1. The gain in stabilization due to the resonance interaction with the p-nitro group is shown by the diminution in the C2-C3 distance with the consequent increase in the C2-C3 bond order and a important localization of the negative charge on the nitro group (-0,4). This is also in agreement with recently proposed Wheland type stabilization in some 2,4,6-trinitro complexes.[24] The C1 angles clearly indicate a σ complex.

In the case of an ortho-substituted complex (Z1b) the results are very sensitive to the criteria followed to diminish the number of variable to be optimized. System B gives smaller total energies than system A, and the results of computation, obtained using system B are then recorded in Table 2. It can be observed that the C1-F and C1-N bonds are similar to those in Z1c compound showing no steric effect of the o-nitro group; the C1 atom is slightly more deviated from the ring plane than in the Z1a and Z1c compounds.

In Table 3 are registered the charge densities for each complex. Examination of the figures reveals an important support of the negative charge by the nitro group which is responsible for the increased stabilization of the complexes, and also a considerable localization of the negative charge on the fluorine atom suggesting an advanced transition state for this reaction. Since this information is not yet available by the present experimental techniques because of the transient nature of these species, the charge distribution shown in Table 3 may be useful in interpreting reactivities and properties of systems in which this kind of complexes may be involved.

Table 3

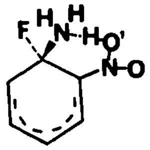
Charge densities[a] for complexes Z1b and Z1c

	Complex Z1b			Complex Z1c		
Method	CNDO	INDO	MNDO	CNDO	INDO	MNDO
Atom						
C1	0.36	0.46	0.41	0.35	0.46	0.36
C2	-0.22	-0.26	-0.40	-0.16	-0.17	-0.27
C3	0.10	0.13	0.14	0.09	0.12	0.11
C4	-0.16	-0.14	-0.28	-0.18	-0.21	-0.36
C5	0.08	0.10	0.03	0.09	0.12	0.11
C6	-0.14	-0.14	-0.20	-0.16	-0.17	-0.27
F	-0.32	-0.39	-0.28	-0.32	-0.38	-0.29
NH_2	-0.13	-0.15	-0.13	-0.15	-0.18	-0.14
NO_2	-0.38	-0.35	-0.41	-0.39	-0.37	-0.41

[a] (electron)

Attack by Ammonia. The next step was to calculate the attack by a neutral nitrogen nucleophile. NAS by amines constitute an important area and the study of their intermediate complexes is very important because of their relevance in the base-catalyzed mechanism of product formation.[25] To minimize the computational time ammonia was chosen as the neutral nucleophile and surprising results were obtained. None of the three Z2 compounds could be calculated by MNDO method: the complexes are not formed and the optimized geometries put the reagents almost 5Å apart. The obtained structures and wave functions correspond to the isolated molecules and the total energies are the sum of the energies of the reagents.

Using CNDO and INDO, compounds Z2a and Z2c were calculated but for compound Z2b the optimized geometry corresponds to an isomer, compound Z2d. For compound Z2d it was necessary to use system B while for Z2a and Z2c system A is good. It can be observed in Table 4 that the complexes have "quasi-aromatic" structures. The low C1-N orders (∿0.5) are consistent with weaker complexes than those given by the amide ion.



Z2d

Table 4

Bond lengths[a] and bond angles[b] for complexes Z2a, Z2d and Z2c

	Comp.	Z2a	Comp.	Z2d	Comp.	Z2c
Method	CNDO	INDO	CNDO	INDO	CNDO	INDO
Bond						
C1-F	1.371	1.384	1.377	1.387	1.369	1.380
C1-N	1.522	1.515	1.437	1.447	1.503	1.501
C1-C2	1.437	1.434	1.494	1.469	1.445	1.443
C1-C6	1.437	1.434	1.467	1.463	1.445	1.443
C2-C3	1.374	1.378	1.423	1.422	1.365	1.369
C5-C6	1.374	1.378	1.343	1.349	1.365	1.369
C3-C4	1.400	1.400	1.351	1.357	1.400	1.400
C4-C5	1.400	1.400	1.429	1.427	1.400	1.400
C1-plane[c]	-0.08	-0.06	0.08	0.10	-0.10	-0.03
$C-NO_2$	-	-	1.37	1.38	1.41	1.41
Angle						
C2-C1-C6	116	116	111	112	115	116
F-C1-N	93	91	101	98	95	93
NO_2-pl.	-	-	4.0	7.0	0.3	0.3

[a] (Å); [b] (°); [c] Positive towards fluorine.

Very interesting is the case of compound Z2d. Its geometry variables and bond orders (close to 1 for C1-N and C1-F) are similar to Z1 complexes. One of the nitrogen hydrogens becomes very close to an oxygen atom of the nitro group, exhibiting an O-H bond order (0.748 (CNDO); 0.572 (INDO)) bigger than the N-H one (0.158 or 0.328). The H-O-N (NO_2) angle is 106° very close to the water molecule angle. This result shows the importance of the hydrogen bond between the ortho-nitro group and the proton in this type of complexes which makes the ortho-nitro derivatives being more reactive than the paraisomers in its reaction with amines,[26,27] while the contrary is observed for anionic nucleophiles. A structure similar to complex Z2d has been previously proposed for the reaction of picryl chloride with secondary amines.[28]

The charge densities show a distribution similar, in a general sense, to the complexes with amide ion. For the reasons given above the results are reported in Table 5.

Table 5

Charge densities[a] for complexes Z2a, Z2d and Z2c

Atom	Comp. Z2a CNDO	Comp. Z2a INDO	Comp. Z2d CNDO	Comp. Z2d INDO	Comp. Z2c CNDO	Comp. Z2c INDO
C1	0.36	0.42	0.34	0.44	0.37	0.43
C2	-0.20	-0.19	-0.17	-0.23	-0.19	-0.19
C6	-0.20	-0.19	-0.10	-0.12	-0.19	-0.19
C3	0.09	0.11	0.08	0.11	0.19	0.13
C5	0.09	0.11	0.07	0.11	0.19	0.13
C4	-0.15	-0.12	-0.07	-0.07	-0.12	-0.14
F	-0.27	-0.33	-0.27	-0.33	-0.26	-0.32
N(NH_3)	0.35	0.36	0.24	0.30	0.42	0.42
N(NO_2)	-	-	0.48	0.60	0.49	0.60
O	-	-	-0.32	-0.35	-0.38	-0.42
O'	-	-	-0.27	-0.37	-0.38	-0.42

[a] (electron)

Heats of Formation. The empirical method of calculation used are not expected to reproduce absolute values for heats of formation but they are good in showing tendencies. The heats of formation for each substrate, reagent and complex were calculated and Table 6 shows the difference between the values for each complex and the corresponding reagents.

Table 6

Heat of Formation Changes[a]

Nucleophile	$NH2^-$			NH3	
Complex	CNDO	INDO	MNDO	CNDO	INDO
Za	-220	-222	-58.8	-53	-67
Zb	-264	-273	-89.9	-116	-125
Zc	-263	-270	-95.0	-67	-81

[a] (kcal/mol)

In all the cases a negative difference was obtained. The difference is bigger for the reaction with the amide ion, which is reasonable since the complex allows a major distribution of the negative charge. For the reaction with ammonia the calculated differences are smaller by CNDO and INDO methods, being very interesting the difference between p- and o-nitrofluoro derivatives. An extra stabilization is observed for the o- isomer which is consistent with the observed greater reactivity of the o-nitro-substituted substrates in its reaction with amines, and with the interpretation of an intramolecular hydrogen bond between the hydrogen of the positively charged amine nitrogen and the oxygen of the nitro group.

The complex "is not formed" by the MNDO technique. This result is not absolutely surprising, and although it prevents calculation of the properties of the complex, it is perhaps more consistent with reality. In fact, all these calculations have been performed without consideration of the solvent effect and there is no evidence that the reaction between ammonia and the studied substrates could occur in the gas phase.

Reaction Coordinates. The failure to find stable complexes by the MNDO calculation could, in principle, be due to the fact that small valleys in the potential energy surface might have been overlooked during the optimization process. Then, the change in the total energy when the reagents are moved from distances corresponding to isolated molecules to bonding distances was examined. The distance Cl-ammonia nitrogen was chosen as the reaction coordinate, this distance was gradually changed as shown in the fig. 1. The rest of the previously considered variable distances were allowed to reach freely the optimum values, including the Cl angles that determine the nucleophile approaching direction. Fig. 1 shows the variation of the heat of formation of complex Z1a and Z2a.

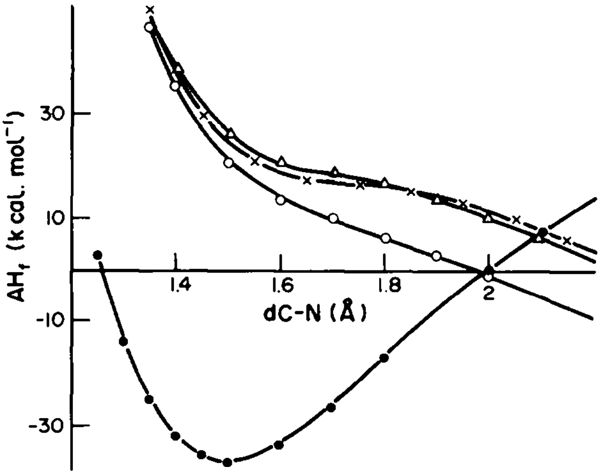


Fig. 1. Heat of formation vs. C-N bond length. Reaction of ammonia with fluorobenzene (O); p-nitrofluorobenzene (Δ); o-nitrofluorobenzene (X) and of fluorobenzene with amide ion (●).

It can be observed that while Z1a shows a deep valley for a Cl-N distance of 1.50Å, no minimum was found for complex Z2a. A somehow different behaviour is exhibited by complexes Z2b and Z2c. Although no local minimum are found, inflexion points are observed in the range 1.7-1.9Å suggesting that if the stabilization due to the solvent were added, local energy minima due to the formation of the complexes could be found in this region for the nitroactivated substrates. Not a reliable theory for a quantitative description of solvent effects[29] have still been developed but inclusion of a few water molecules near the charged centres produces an energy decrease.[30] A more detailed application of some techniques to include solvent interaction is in progress. Nevertheless, the more critical mechanistic controversias are for reactions ocurrying in non-polar solvents.[31]

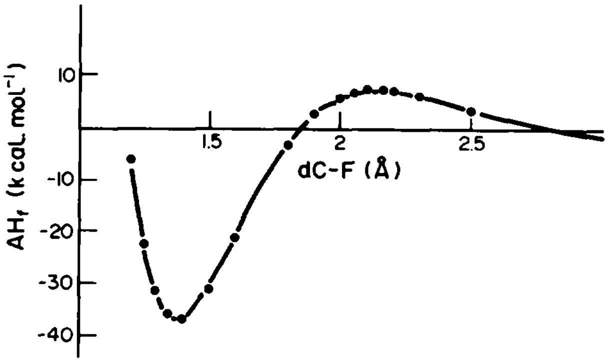


Fig. 2. Heat of formation vs. C-F bond length. Reaction of fluorobenzene with amide ion.

Finally, the reaction coordinate of the leaving group departure was studied for complex 21a, till 5Å Cl-F distance. It can be observed in fig. 2 that the energy maximum occurs ar 2.14Å. It is also interesting to observe a species that has a smaller energy than the sum of the isolated molecules ocurrying at a Cl-F distance of 3.81Å. There is no apreciable bond interaction between both molecules except a slight charge transfer from the fluoride to the aniline molecule. It is expected that for nitro-activated substrates the charge transfer should be bigger.

CONCLUSIONS

The level of agreement obtained between de present calculations and the qualitative expectations based on experimental results obtained with stable Meisenheimer complexes allows the prediction of properties for model systems that are not amenable to experiment yet. Data for bond length, bond angles, dihedral angles, bond orders and charge densities, for the complexes between fluorobenzene, p- and o-fluoro-nitrobenzene with amide ion or ammonia were calculated by appropiate procedures to produce an almost complete optimization of the geometries. The obtained results show that they can greatly help our understanding of the mechanisms of formation and decomposition of these important intermediate complexes. A similar study of more substituted stable compounds is in progress, the results are compared with NMR(^{1}H, ^{13}C) and X-ray diffraction studies.

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