SUBSTITUENT EFFECTS ON PROTON AFFINITIES : THROUGH BONDS OR THROUGH SPACE
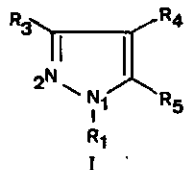MECHANISM?

Javier Catalán* and Pilar Pérez

Departamento de Química Física y Química Cuántica, Facultad de Ciencias,
C-XIV, Universidad Autónoma de Madrid, Cantoblanco, Madrid-34, Spain

José Elguero

Instituto de Química Médica, CSIC, Juan de la Cierva 3, Madrid-6, Spain

Abstract - INDO calculations of the protonation energies and lone pair orbi-
tal energies of twenty pyrazoles and twenty imidazoles have been carried out
in order to ascertain the mechanism of the substituent effect. Methyl, cyano,
fluoro, amino, and nitro substituents have been examined. The last one shows
a special behaviour. The importance to optimize the geometry and the reasons
for the anomaly shown by the nitro derivatives are discussed.

In 1981 Gribov et al.[1] restated the problem of the mechanism of transmission of polar substituent
effects.[2] Even for small molecular systems, where the substituent and the reaction centre are near
(separated by one or two bonds), they assumed that the transmission is essentially through space.
Their conclusion is mostly based on the fact that calculated total charge densities of ring atoms
for pairs like nitrobenzene-benzene, phenol-benzene, etc. hardly change whereas the calculated
electrostatic potentials of nitrobenzene and phenol are clearly different from that of benzene.
Due to this fact, they rejected a mechanism of transmission through-the-bonds, even in aromatic
systems, as the main factor for the modification of reactivity produced by polar substituents.
More recently, the same authors[3] have analyzed the effect of polar substituents on the calculated
(CNDO) protonation energies ΔE_p of pyrazoles I. Stressing on the aforementioned ideas, they
pointed out that the depth of the minimun of the molecular electrostatic
potential (which is located near N_2, the basic centre of pyrazole) is li-
nearly related with ΔE_p, whereas the total charge of the basic centre,
q_{N_2}, does not show any correlation with the protonation energy ($r^2 = 0.117$).
Thus they conclude again that there is no relationship between the reacti-
vity and any property located on the basic centre N_2.

We do not think that the arguments given by Gribov are sound, particularly if we take into account
the fact that q_{N_2} (total) includes molecular orbitals not directly implicated in the protonation
process. These MO change from one compound to another, especially in the pyrazole family where the
basic centre N_2 is contiguous to the pyrrolic nitrogen N_1. As a matter of fact, other magnitudes
are more adequate for this type of analysis. For instance, the existence of linear relationships
between the proton affinity and the (1s) inner-shell ionization energies[4-12] or between the former
and the valence-shell ionization energies is well established.[8,12-18] The fact that substituents
produce appreciable modifications on the above energies, even when they are located far from the
basic centre is also well documented.[19-23]
Gribov et al.[3] assume that the influence of the reorganization of the molecular geometry produced
by the substituent is negligible. Our opinion radically differs from that of Gribov, especially in

comparative problems like those of substituent effects on pyrazole proton affinities. It has been shown by Coulson et al.[24] that the substituent produced geometrical modifications of the ring due to hybridation effects, valence-shell electron-pair repulsions, intramolecular nonbonded interactions and coulombic interactions between formally charged atoms. INDO method on fully optimized geometries has given satisfactory results on similar problems.[25-27] If the same pyrazoles as those studied by Gribov et al.[3] are calculated using the INDO procedure on optimized geometries, the correlation between ΔE_p and q_{N_2} increases from $r^2 = 0.117$ to $r^2 = 0.565$, indicating that, contrary to Gribov's conclusions, there is some relationship between the protonation energy and the total charge of the basic centre.[28]

In the preceding paper of these series[29] we have shown that for parent diazoles (pyrazoles I and imidazoles II) and their methyl derivatives there is a linear correlation between the protonation energies ΔE_p and the lone pair orbital energies ε_N (N_2 in pyrazoles and N_3 in imidazoles). Forty pyrazoles and imidazoles bearing different substituents (CH_3, CN, NH_2, NO_2, F)[30] have been calculated within the INDO approximation. All the geometries were optimized; the three atoms of the nitro group lie in the diazole plane but the hydrogen atoms of the amino group were free to adopt the more stable geometry (both below the plane of the diazole forming a flattened pyramid). The protonation energies ΔE_p (in kcal.mole^{-1}) and the orbital energies ε_N (in a.u.) are gathered in the following table.
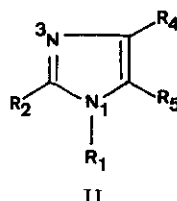
TABLE. Protonation energies (kcal.mole^{-1}) and lone pair orbital energies (a.u.)

	Pyrazoles							Imidazoles					
№	R_1	R_3	R_4	R_5	ΔE_p	ε_N	№	R_1	R_2	R_4	R_5	ΔE_p	ε_N
1	H	H	H	H	355.7	0.4788	21	H	H	H	H	368.5	0.4577
2	H	CH_3	H	H	363.7	0.4675	22	H	H	CH_3	H	373.7	0.4475
3	H	H	H	CH_3	362.4	0.4731	23	H	H	H	CH_3	371.3	0.4570
4	H	H	CH_3	H	356.9	0.4769	24	H	CH_3	H	H	378.0	0.4444
5	H	CH_3	H	CH_3	369.7	0.4621	25	H	H	CH_3	CH_3	375.8	0.4475
6	H	CH_3	CH_3	H	364.1	0.4657	26	H	CH_3	CH_3	H	382.7	0.4357
7	H	H	CH_3	CH_3	363.4	0.4716	27	H	CH_3	H	CH_3	380.2	0.4443
8	H	CH_2	CH_3	CH_3	369.3	0.4599	28	H	CH_3	CH_3	CH_3	384.3	0.4357
9	CH_3	H	H	H	360.1	0.4735	29	CH_3	H	H	H	370.6	0.4606
10	CH_3	CH_3	H	H	367.4	0.4627	30	H	NH_2	H	H	384.7	0.4420
11	CH_3	H	H	CH_3	366.0	0.4686	31	H	H	H	NH_2	374.9	0.4482
12	CH_3	H	CH_3	CH_3	361.1	0.4724	32	H	H	H	F	358.3	0.4690
13	CH_3	CH_3	H	CH_3	372.7	0.4571	33	H	H	H	CN	360.9	0.4727
14	H	H	NH_2	H	358.7	0.4729	34	H	H	NO_2	H	345.7	0.5111
15	H	H	F	H	342.9	0.4925	35	H	H	H	NO_2	345.3	0.5128
16	H	H	H	F	349.0	0.4883	36	H	NO_2	H	H	343.7	0.5113
17	H	H	CN	H	348.6	0.4885	37	H	CH_3	NO_2	H	356.3	0.4989
18	H	H	H	CN	350.2	0.4905	38	N	CH_3	H	NO_2	355.6	0.5008
19	H	H	NO_2	H	331.9	0.5285	39	CH_3	H	NO_2	H	348.0	0.5112
20	H	H	H	NO_2	331.9	0.5294	40	CH_3	H	H	NO_2	348.3	0.5085
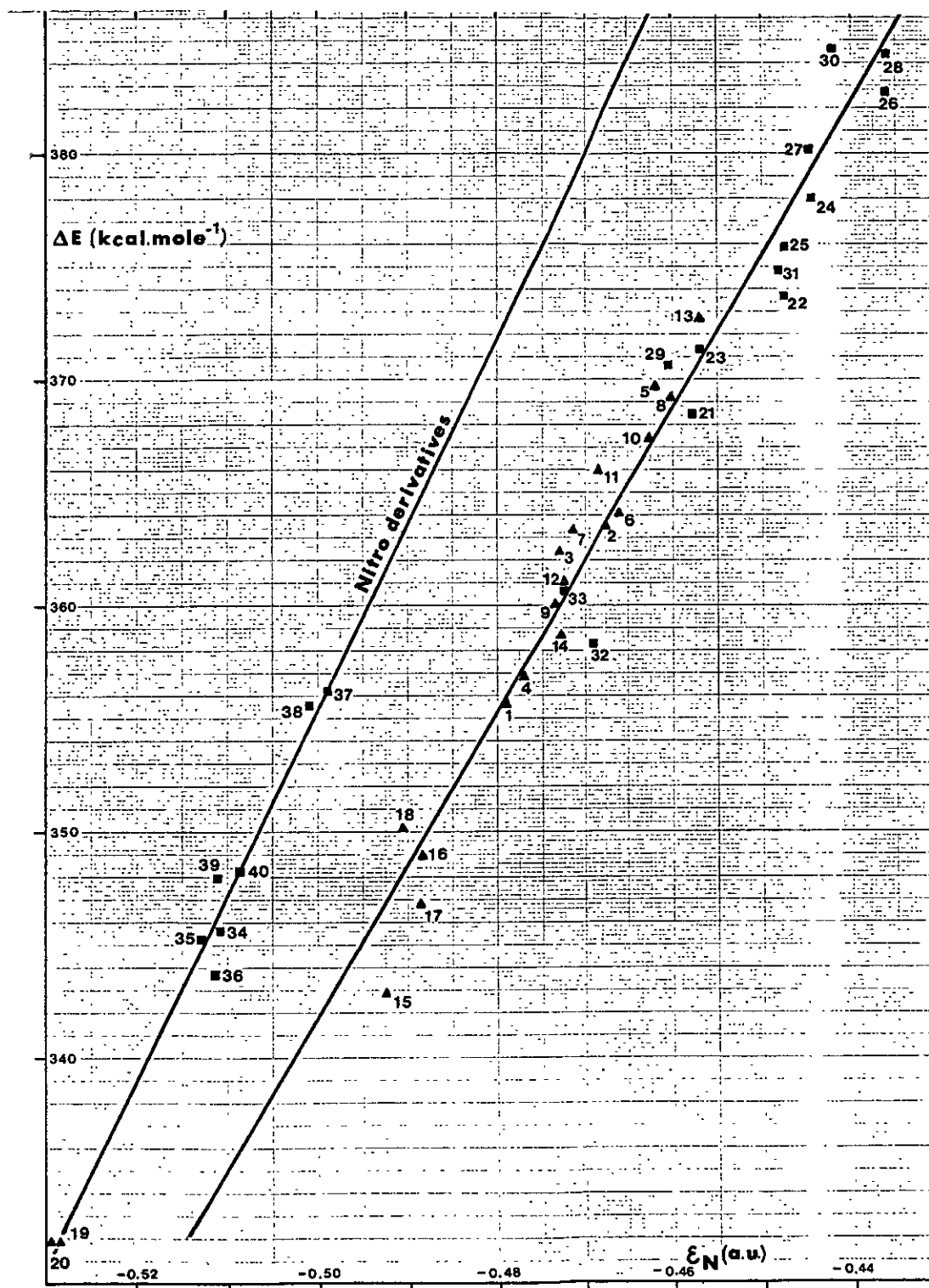
A representation of ΔE_p vs ε_N is given in the preceding figure. Clearly two families of deriva-
tives are present: that including all the compounds (Pyrazoles ▲ and imidazoles ■) but the nitro
derivatives (Eq. 1) and the nitropyrazoles (▲) and nitroimidazoles (■) family (Eq. 2).

$$\Delta E_p = 679.6 + 675.9 \ \varepsilon_N, \ n = 31, \ r^2 = 0.963 \quad [1]$$
$$\Delta E_p = 765.3 + 819.7 \ \varepsilon_N, \ n = 9, \ r^2 = 0.982 \quad [2]$$

The nitro derivatives set includes compounds with the nitro group in the α position to the basic
centre (N_2 in pyrazoles and N_3 in imidazoles) 34, 36, 37, 39, and in the β position, 19, 20, 35,
38, 40.

These results deserve some comments:

      - The fact that the correlation between ΔE_p and q_N improves when the geometries are
optimized cats a doubt on Gribov's conclusions.

      - The excellent agreement between ΔE_p and ε_N shows that a property located on the
basic centre conveniently describes the modification of the reactivity of that centre produced by
the polar substituent.

      - Trying to understand why the nitro derivatives lie aside we have observed that the
orbital located on the nitrogen lone pair and on the nitro group are very close (the second one
slightly more energetic) and this results in some mixing. Thus, the calculated ε_N values are too
large (approximately -0.02 a.u., from the figure).

REFERENCES AND NOTES
1.   L.A. Gribov and S.B. Savvin, J. Mol. Struct., 1981, 71, 263.
2.   S. Ehrenson, Prog. Phys. Org. Chem., 1964, 2, 195; L.S. Levitt and H.F. Widing, Prog. Phys.
     Org. Chem., 1976, 12, 119.
3.   L.A. Gribov, S.B. Savvin, M.M. Reichstat, and M.Yu. Orlov, J. Mol. Struct., Theochem, 1982,
     88, 171.
4.   R.L. Martin and D.H. Shirley, J. Amer. Chem. Soc., 1974, 96, 5299.
5.   D.W. Davis and J.W. Rabelais, J. Amer. Chem. Soc., 1974, 96, 5305.
6.   B.E. Mills, R.L. Martin, and D.A. Shirley, J. Amer. Chem. Soc., 1976, 98, 2380.
7.   R.G. Cavell and D.A. Allison, J. Amer. Chem. Soc., 1977, 99, 4201.
8.   F.M. Benoit and A.G. Harrison, J. Amer. Chem. Soc., 1977, 99, 3980.
9.   S.R. Smith and T.D. Thomas, J. Amer. Chem. Soc., 1978, 100, 5459.
10.   T.H. Lee, W.L. Jolly, A.A. Bakke, R. Weissand, and J.G. Verkade, J. Amer. Chem. Soc., 1980,
     102, 2631.
11.   J.M. Buschek, F.S. Jorgensen, and R.S. Brown, J. Amer. Chem. Soc., 1982, 104, 5019.
12.   J. Catalán, O. Mo, P. Pérez, and M. Yañez, J. Chem. Soc. Perkin Trans. II, 1982, 1409.
13.   J.L. Beauchamp, M. Caserio, and T.B. McMahon, J. Amer. Chem. Soc., 1974, 96, 6241.
14.   D.H. Aue, H.M. Webb, and M.T. Bowers, J. Amer. Chem. Soc., 1975, 97, 4136.
15.   W.G. Henderson, D.H. Taagepera, R.T. McIver, J.L. Beauchamp, and R.W. Taft, J. Amer. Chem.
     Soc., 1972, 94, 4729.
16.   R.H. Staley, J.E. Kleckner, and J.L. Beauchamp, J. Amer. Chem. Soc., 1976, 98, 2081.
17.   M. Meot-Ner (Mautner), J. Phys. Chem.,1980, 84, 2716.
18.   R.L. Dekock and M.R. Barbachyn, J. Amer. Chem. Soc., 1979, 101, 6156.
19.   J. Catalán and M. Yañez, Chem. Phys. Lett., 1979, 60, 499.
20.   D.W. Turner, C. Baker, A.D. Baker and C.R. Brundle, 'Molecular Phothoelectron Spectroscopy',
     Wiley-Interscience, New York, 1970.
21.   T. Kobayashi and S. Nagakura, Bull. Chem. Soc. Jpn., 1974, 47, 2563.
22.   M.N. Palmer, W. Moyes, M. Spiers, and J.N. Ridyard, J. Mol. Struct., 1978, 49, 105; 1979, 52,
     293; 1979, 53, 235, and 1979, 55, 243.
23.   L. Klasing, B. Rusciv, G. Heinrich, and F. Gusten, Z. Naturforsch., 1977, 32b, 1291.
24.   A. Domenicano, A. Vaciano, and C.A. Coulson, Acta Cryst., 1975, B31, 221.
25.   J. Catalán and A. Macias, J. Mol. Struct., 1977, 38, 209.
26.   J. Catalán, P. Pérez, and M. Yañez, Tetrahedron, 1982, 38, 3693.
27.   J. Catalán, O. Mo, P.Pérez, and M. Yañez, a) J. Mol. Struct., Theochem, in press; b) Tetra-
     hedron, in press.
28.   J. Catalán, J. de Paz, M. Yañez, and J. Elguero, unpublished results.
29.   This work is Part III of 'Basicity of Azoles'. For preceding parts, see J. Catalán and J. El-
     guero, J. Chem. Soc. Perkin Trans. II, submitted for publication and Angew. Chem. Int. Ed.
     Engl., in press.
30.   This set of twenty pyrazoles includes all the compounds studied by Gribov et al.