

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

Javier Catalán* and Pilar Pérez

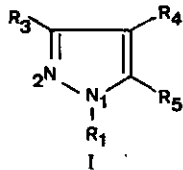
Departamento de Química Física y Química Cuántica, Facultad de Ciencias,
C-XIV, Universidad Autónoma de Madrid, Cantoblanco, Madrid-34, Spain

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 orbital 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 authors³ 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 minimum of the molecular electrostatic potential (which is located near N_2 , the basic centre of pyrazole) is linearly 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 reactivity 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 energies⁴⁻¹² 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 series²⁹ 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.

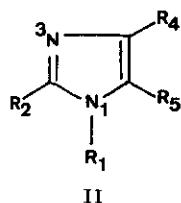
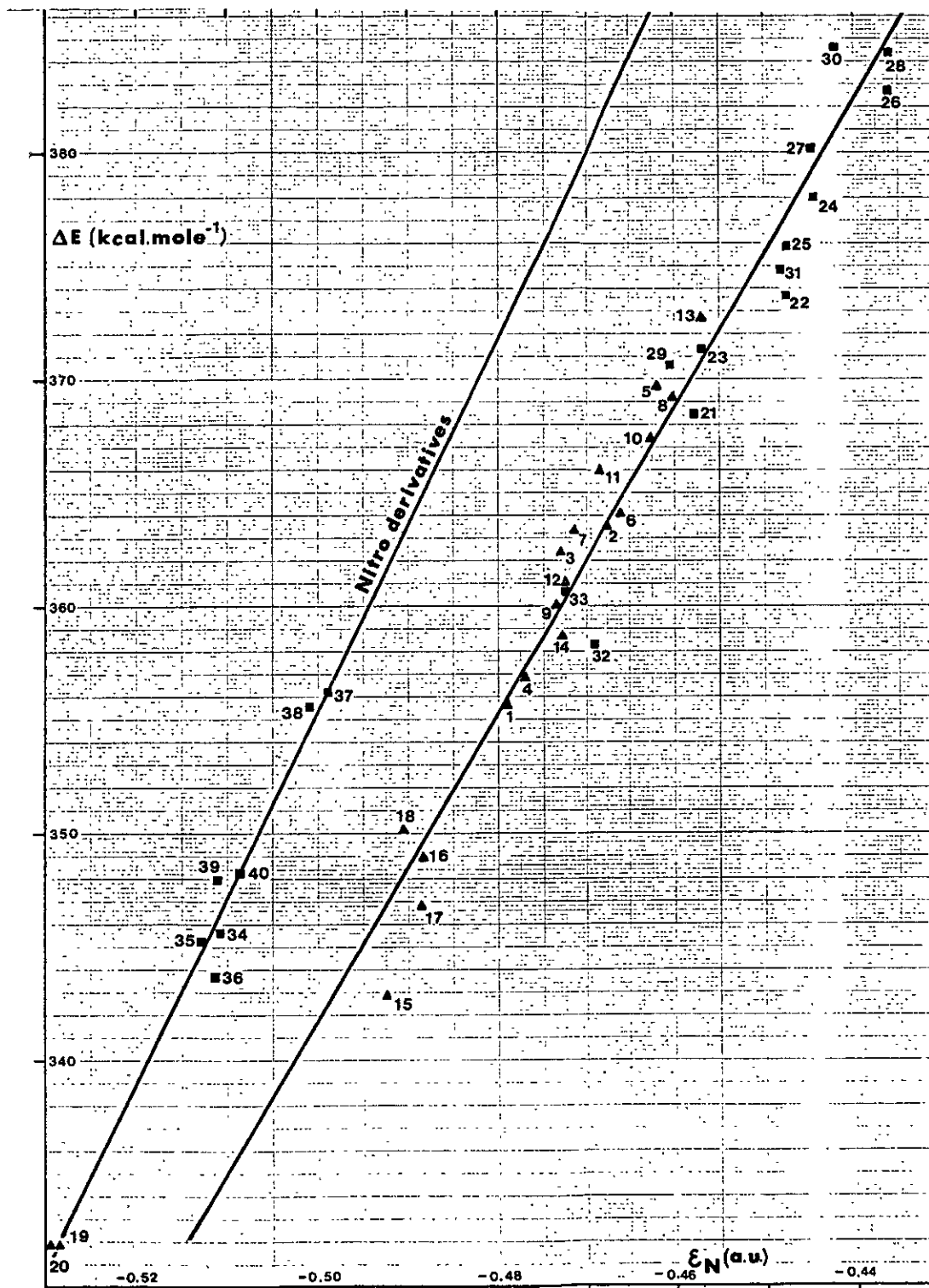


TABLE. Protonation energies (kcal.mole⁻¹) and lone pair orbital energies (a.u.)

Pyrazoles							Imidazoles						
Nº	R ₁	R ₃	R ₄	R ₅	ΔE_p	ϵ_N	Nº	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 derivatives are present: that including all the compounds (Pyrazoles \blacktriangle and imidazoles \blacksquare) but the nitro derivatives (Eq. 1) and the nitropyrazoles (\blacktriangle) and nitroimidazoles (\blacksquare) family (Eq. 2).

$$\Delta E_p = 679.6 + 675.9 \epsilon_N, n = 31, r^2 = 0.963 \quad [1]$$

$$\Delta E_p = 765.3 + 819.7 \epsilon_N, n = 9, r^2 = 0.982 \quad [2]$$

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 casts 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. Rabalais, *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. Ave, 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. Kieckner, 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 Photoelectron Spectroscopy', Wiley-Interscience, New York, 1970.
21. T. Kobayashi and S. Nagakura, *Bull. Chem. Soc. Jpn.*, 1974, 47, 2563.
22. M.H. 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) *Tetrahedron*, 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. Elguero, *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.*

Received, 8th April, 1983