Tetrahedron Letters No. 7, pp 639 - 642.
© Pergamon Press Ltd. 1979. Printed in Great Britain.

0040-4039/79/0208-0639$02.00/0

ANALYSIS OF TORSIONAL BARRIERS IN AMIDES AND THIOAMIDES BY THE PMO METHOD

Jan Sandström

Division of Organic Chemistry 1, Chemical Center,
University of Lund, S-220 07 Lund 7, Sweden

Bingham[1] has discussed the stabilizations arising in organic molecules through interaction between a lone pair on a donor atom and the σ^* orbital in a vicinal polar bond.[2] In the PMO treatment with neglect of overlap[3] the stabilization ΔE is given by (1),

$$\Delta E = \frac{2H_{ij}^2}{\Delta\varepsilon_{ij}} \qquad (1)$$

where H_{ij} is the matrix element between the interacting orbitals and $\Delta\varepsilon_{ij}$ is their energy separation.

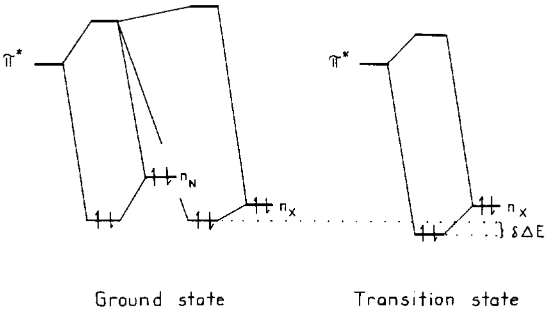
Among Bingham's illustrations are the torsional barriers in N,N-dimethylcarbamoyl halides, X-CO-NMe_2. The barriers decrease in the sequence X = F, Cl, Br (Table), and this is ascribed to a stabilizing interaction between the lone pair orbital on nitrogen and the σ^* orbital in the C-X bond in the transition state. The σ^* energy is assumed to decrease in the above sequence.

More recently, Kost and Kornberg[4] have analysed the effect of a para nitro group on the torsional barrier in N,N-dimethyl-o-phenylcarbamate in the same terms. The nitro group raises the barrier by 0.6 kcal mol^{-1}, whereas it was expected, by lowering the σ^* orbital and thereby diminishing $\Delta\varepsilon_{ij}$, to lower the energy of the transition state and thus the barrier. Kost and Kornberg explain the barrier-raising effect of the nitro group as a stabilization of the ground state alone.

It seems as if these observations as well as the general effect of donor groups X on the torsional barriers in amides, X-CO-NR_2, and thioamides, X-CS-NR_2, can be coherently analysed in terms of the interaction of the lone pair orbital of the donor group X and the π^* orbital of the (thio)carbonyl group in the ground state and in the transition state.[5] This statement is based on the observation that the matrix elements $|H_{ij}|$ are larger and the energy gaps $\Delta\varepsilon_{ij}$ smaller for the $n_X-\pi^*_{C=O}$ interaction than for the $n_N-\sigma^*_{C-X}$ interaction.

The strong $n_N-\pi^*_{C=O}$ interaction in a planar amide should raise the π^* level considerably, whereas in the transition state this level should remain approximately unperturbed. Therefore, ΔE due to the $n_X-\pi^*_{C=O}$ interaction should be larger in the transition state than in the ground state (Figure), and the difference $\delta\Delta E = \Delta E_{tr} - \Delta E_{gr}$ is given by (2) and expected to increase with increasing n_X

$$\delta\Delta E = 2H_{ij}^2 \left(\frac{1}{\Delta\varepsilon_{ij}^{tr}} - \frac{1}{\Delta\varepsilon_{ij}^{gr}}\right) \qquad (2)$$



Figure

energy. The n_X energies should come in the same order as negative ionization potentials of HX. The variations in the matrix elements are probably of minor importance.[6]

An inspection of the Table shows that the above predictions are very well borne out by the experimental barriers.

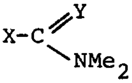
The torsional barriers in thioamides are in general 1-3 kcal mol^{-1} higher than in the corresponding amides.[17] In the present model this is explained by the lower π^* level in C=S than in C=O.[18] This gives a larger ΔE term for the interaction $n_N-\pi^*$, which is an approximation to the barrier. Furthermore, a lower π^* level leads to smaller $n_X-\pi^*$ energy gaps, the $\delta\Delta E$ values should be larger in thioamides than in amides. This is seen to be the case (Table), and it is also borne out by the statistical analysis performed by Piccinni-Leopardi et al.[17] on 20 amide-thioamide pairs, which gave the equation (3) with the correlation coefficient r = 0.97.

$$\Delta G^{\ddagger}(\text{thioamide}) = 1.13 + 1.11\,\Delta G^{\ddagger}(\text{amide}) \qquad (3)$$

This model also allows an interpretation of the effects on torsional barriers of substituents, which modify the donor capacity of the nitrogen atom.

Piccinni-Leopardi et al.[17] have used the $n_N-\pi^*$ interaction model to explain the difference in barrier between (thio)piperidides and (thio)morpholides. The lower barriers in the morpholides correlate nicely with the ionization potentials in morpholine and piperidine, 8.91 eV and 8.66 eV, respectively. Larger effects, such as the low barriers in N-vinylamides[19] and N-fluoroamides[20] are also encompassed by the $n_N-\pi^*$ interaction model.

Table

Torsional barriers ($\Delta G_c^{\ddagger}$) of  $X{-}C({=}Y)NMe_2$ and ionization potentials (I_p) of HX

X	Y	$\Delta G^{\ddagger}$ kcal mol^{-1}	Ref	Ip eV	Ref
H O	O	20.9	7		
F	O	18.2	8	15.77	9
Cl	O	16.7	8	12.74	9
Br	O	15.7	8	11.62	9
CH_3O	O	15.1	11	10.94	10
C_6H_5O	O	16.5	4		
$p-O_2NC_6H_4O$	O	17.1	4		
$2-C_3H_7NH$	O	9.7	12	9.31	10
H	S	24.1	13		
F	S	20.7	14		
Cl	S	18.7	14		
CH_3O	S	17.7	15		
CH_3NH	S	10.6	16	9.64	10

Acknowledgement. Financial support from the Swedish Natural Science Research Council is gratefully acknowledged.

REFERENCES

1. R.C. Bingham, J. Am. Chem. Soc. **97**, 6743 (1975).
2. R. Hoffmann, L. Radom, J.A. Pople, P.v.R. Schleyer, W.J. Hehre and L. Salem, J. Am. Chem. Soc. **94**, 6221 (1972).
3. N.D. Epiotis, W.R. Cherry, S. Shaik, R.L. Yates and F. Bernardi, Top. Cur. Chem. **70**, 1 (1977).
4. D. Kost and N. Kornberg, Tetrahedron Lett. **1978**, 3275.
5. Presented at the 8th International Symposium on Organic Sulphur Chemistry in

Portoroz, Yugoslavia, June 1978.

6. See e.g. the C-F, C-O and C-Cl overlap integrals in Ref. 3, p. 20.
7. M. Rabinovitch and A. Pines, *J. Am. Chem. Soc.* **91**, 1585 (1969).
8. E.A. Allan, R.F. Hobson, L.W. Reeves and K.N. Shaw, *J. Am. Chem. Soc.* **94**, 6604 (1972).
9. A.J. Gordon and R.A. Ford, *The Chemists Companion*, Wiley, New York 1972, p. 237.
10. S. Katsumata, T. Iwai and K. Kimura, *Bull. Chem. Soc. Japan* **46**, 3391 (1973)
11. S. Henriksson and J. Sandström, to be published.
12. P. Stilbs, *Acta Chem. Scand.* **25**, 2635 (1971).
13. T.H. Siddall III, W.E. Stewart and F.C. Knight, *J. Phys. Chem.* **74**, 3580 (1970).
14. R.F. Hobson, L.W. Reeves and K.N. Shaw, *J. Phys. Chem.* **77**, 1228 (1973).
15. J. Sandström, *J. Phys. Chem.* **71**, 2318 (1967).
16. G. Isaksson and J. Sandström, *Acta Chem. Scand.* **24**, 2565 (1970).
17. C. Piccinni-Leopardi, O. Fabre, D. Zimmermann and J. Reisse, *Can. J. Chem.* **55**, 2649 (1977).
18. F. Bernardi, L. Lunazzi, P. Zanirato and G. Cerioni, *Tetrahedron* **33**, 1343 (1977).
19. D.G. Gehring, W.A. Mosher and G.S. Reddy, *J. Org. Chem.* **31**, 3436 (1966).
20. J. Cantacuzene, J. Leroy, R. Jantzen and F. Dudragne, *J. Am. Chem. Soc.* **94**, 7924 (1972).

(Received in UK 8 December 1978)