Theoretical Studies of Substituent Effects on Stationary Structures of Amidine Decomposition

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The unimolecular decomposition of substituted acetamidines XC(=NH)NH_2, where X = CH_3(I), CH_2F (II), CHF_2 (III), CF_3 (IV), CH_2NH_2 (V) and CH_2NO_2 (VI) has been examined by *ab initio* methods using the 4-31G standard basis set. The process has an asynchronous mechanism. Transition structures for all the compounds can be described as four-membered rings. The influence of substitution on the decomposition process is discussed in terms of a modified version of a More O'Ferrall–Jencks type diagram. The effects of functional groups are larger in a perpendicular than a parallel orientation to the reaction path; this is an example of the 'anti-Hammond' effect.

Amidines and related compounds such as guanidines and iso(thio)ureas are good models on which to study the active centre of the enzyme lactate dehydrogenase[1] and other enzymes[2] where the guanidinium group of arginine plays an important role in substrate fixation. In our previous synthetic[3] as well as X-ray[4] communications we devoted considerable effort to an experimental investigation of this interaction. Amidines have been known for years to decompose at elevated temperatures to yield nitriles and ammonia. Equilibrium between amidines and respective nitriles has been frequently observed[5] and some experimental results suggests that the decomposition of amidines is a unimolecular process.[6] In our previous theoretical communications we focused on the unimolecular decomposition of formamidine[7] and examined the reliability of various basis sets to describe this process in the case of acetamidine.[8] According to our previous knowledge, the decomposition mechanism of amidines to ammonia and respective nitriles *in vacuo* can be described as a single step taking place *via* a four-centred transition state. The inverse process may also be interpreted in terms of ammonia addition to the respective nitriles and compared to similar results which have been observed for different addition reactions by various authors.[9] Due to interest in the amidine unimolecular decomposition, we now decided to perform a comprehensive examination of this reaction for a family of such compounds bearing different substituents in order to get a theoretically-based confirmation of the decomposition nature.

The determination of the mechanism and calculation of the energetics and rates of chemical reactions requires, first of all, the characterization of the potential energy surface (PES) for the composite molecular system of interest. The theoretical treatment of chemical reactivity using the PES should focus on stationary point structures: reactants (R), products (P), intermediates (if any) and the transition state (TS).

From a technical point of view, R and P can be calculated routinely, reliably and accurately.[10] In principle, TS can be calculated equally well though in practice it requires greater skill to search for than equilibrium geometries. A variety of efficient algorithms are now available for TS searches,[11] thus providing a range of powerful tools for the design, exploration and characterization of potential energy surfaces for chemically reacting systems. However, the location and characterization of transition structures is at present far from routine.

The details of the critical points of chemical reaction surfaces may change at higher levels of theory (*e.g.* larger basis sets and/or inclusion of electron correlation), but it is not our present aim to provide a quantitatively accurate description of these energy surfaces. In our preliminary study[8] we evaluated the basis sets effect on stationary structures of acetamidine decomposition and we found that the fundamental features of the reaction path are quite well represented when the calculations are performed with a double-zeta basis set (4-31G) as compared with calculations with substantially higher levels of sophistication.

In the present paper, we report results of an investigation of more complicated amidines with the aim of clarifying the influence of different substituents on the unimolecular decomposition process. We decided to deal with substituted acetamidines, which allow calculations to be performed at a rather sophisticated level, but which also permit systematic variation of the molecule substitution. Thus acetamidine (I), its fluoro-analogues (II–IV) and compounds arising from substitution by the amino (V) as well as the nitro group (VI) were investigated.

Calculations.—All calculations were performed on an IBM 3090/150 computer at the *Centre d'Informàtica de la Universitat de Valencia* using the MONSTERGAUSS program.[12] Analytical gradients[13] of the SCF HF energy with respect to the internal geometric parameters were calculated and the optimally conditioned (OC) minimization technique[14] was

Table 1 4-31G optimized reacting bond lengths/Å for reactants, transition states and products in the decomposition of amidines I–VI. Δ(C–N1) and Δ(C–N2) are the absolute differences between the values of the bond distances C–N1 and C–N2, respectively.

	I	II	III	V	V	VI
Reactants						
C–N1	1.254	1.265	1.261	1.254	1.269	1.249
C–N2	1.430	1.356	1.357	1.359	1.356	1.408
N2–Ht	2.430	2.580	2.588	2.595	2.554	2.488
Transition states						
C–N1	1.239	1.241	1.242	1.243	1.239	1.239
C–N2	1.577	1.524	1.514	1.500	1.568	1.521
N2–Ht	1.266	1.280	1.286	1.293	1.269	1.282
Δ(C–N1)	0.02	0.02	0.02	0.01	0.03	0.01
Δ(C–N2)	0.14	0.16	0.15	0.14	0.21	0.11
Products						
C–N1	1.143	1.140	1.138	1.136	1.143	1.139
N2–Ht	0.994	0.991	0.997	0.993	0.993	0.986

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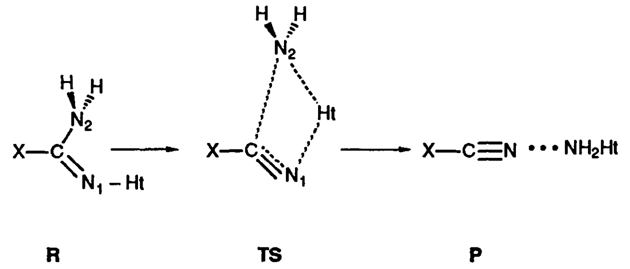
Table 2 Components of the transition vector for the TS calculated for compounds I–VI by means of the 4-31G basis set. Force constants (mdyn Å^{-1} or mdyn rad^{-1} are given in parentheses.

Compound	Eigenvalue	C–N1	C–N2	Ht–N2	N1–C–C	N2–C–N1	Ht–N2–N1
I	−4.631	−0.025	0.367	0.735	−0.074	0.183	0.532
		(12.984)	(1.537)	(−0.949)	(1.592)	(3.430)	(1.009)
II	−4.528	−0.014	0.316	0.740	−0.076	0.198	0.553
		(12.851)	(2.320)	(−0.943)	(1.500)	(3.297)	(0.989)
III	−4.458	−0.005	0.298	0.743	−0.071	0.194	0.561
		(12.824)	(2.655)	(−0.913)	(1.535)	(3.385)	(0.985)
IV	−4.423	−0.003	0.283	0.746	−0.066	0.193	0.565
		(12.734)	(2.986)	(−0.920)	(1.592)	(3.349)	(0.989)
V	−4.669	−0.033	0.376	0.737	−0.084	0.197	0.517
		(12.946)	(1.389)	(−1.017)	(1.573)	(3.392)	(1.109)
VI	−4.481	−0.013	0.316	0.745	−0.063	0.190	0.551
		(12.954)	(2.374)	(−0.945)	(1.663)	(3.458)	(1.023)



	X
I	CH_3
II	CH_2F
III	CHF_2
IV	CF_3
V	CH_2NH_2
VI	CH_2NO_2

Fig. 1 Schematic representation of the stationary points R, TS and P for the unimolecular decomposition of substituted acetamidines I–VI

used to determinate the minimum-energy profiles. The transition states were located with the VA05 subroutine[15] and the transition vector was determined by diagonalizing the force constant matrix. The exact characterization of the TS was achieved by utilization of the control-space approach.[16] The TS geometries originated in those investigated recently[7,8] and were optimized first by a VA05 method restricted to control space (variables which participate in the transition vector). As a second step we optimized the complementary space-utilizing method, OC. Finally, a complete optimization with the use of the VA05 method was achieved for the complete space of all variables. The optimizations were terminated after the overall average gradient length had been reduced to $< 5 \times 10^{-4}$ mdyn.

Results and Discussion

The stationary points R, TS and P in the global process of substituted amidine decomposition are depicted in Fig. 1. Selected structural parameters for the optimized reactants, transition states and products are listed in Table 1. The geometries of all compounds do not differ substantially among themselves in the respective stationary points and the total geometry is available as Supplementary data [sup. no. 56808 (4 pp.)].* The angle Ht–N1–N2 is *ca.* 22.7–24.2° for the reactant geometries, and this value increases to 37.7–38.9° in the TS geometries. The products may be described as supermolecules composed of ammonia and the respective nitrile and variations of this angle in the product geometries are of low importance because they now refer to the ammonia orientation, which can vary substantially. It is important to note that the TS for the amino functional group, **V**, has superior absolute values for Δ(C–N2) and Δ(C–N1) than the remainder of the substituents; then a TS near the products is attained for **V**. Thus the electron-donating groups advance the TS position along the reaction pathway while the electron-withdrawing groups retard it. These results are not sensitive to the basis set used.[8]

Another possibility with which to compare the similarity of transition-state structures is given in Table 2, where the components of the transition vectors for the TS calculated for compounds **I–VI** are presented. We note that the magnitude of the eigenvalue, which is related to the curvature of the energy surface, is remarkably constant. To distinguish which variables control the decomposition process we analysed these transition vectors. From all the variables only four contribute > 10%, and among them the forming N2–Ht and breaking C–N2 bonds are predominant together with the Ht position described by angle Ht–N2–N1. The force constants for Ht–N2 are negative. The force constant values for the C–N2 variable has a minimum for **V**; this fact confirms that the TS for this substituent is the most advanced along the reaction pathways, in agreement with the variation of geometry pointed out in Table 1.

Table 3 summarizes the activation and reaction energies for the decomposition processes. There is no regular relation between the activation and the reaction energy for the amidine decomposition to ammonia and nitrile. Thus the classical Hammond postulate[17] does not hold for these reactions. The difference in activation energy amounts to *ca.* 16 kcal mol^{-1} corresponding to a rate ratio of *ca.* 10^{12} between reactions of compounds **I** and **V**.

Bond orders are used as a measure of the reaction progress in theories of structure-reactivity correlations[18] in order to search the similarity of the TS structure for a family of compounds. Recently, Lendvay[19] remarked on the importance of bond order rearrangement in the study of theoretical chemical reactions. To follow the nature of the reaction we have employed a More O'Ferrall–Jencks type diagram.[20] In Fig. 2 a modified version of this diagram in terms of the Mayer bond orders[21] of the reacting bonds is shown. The lower-left corner represents the reactants and the upper-right corner the products and the upper-left and lower-right corners correspond to hypothetical intermediate structures. The reactions follow lines connecting the positions of the R, TS and P. A diagonal connection between R and P represents a synchronous process, and the opposite corners represents a stepwise mechanism. It is important to note that the abscissae for all R, TS and P,

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* *Supplementary Data:* for details of the deposition scheme, see 'Instructions for Authors' (1991), *J. Chem. Soc., Perkin Trans. 2*, in the January issue.

Table 3 Energy of reactants, TS and products, respectively (in Hartrees) calculated for compounds **I–VI** at the 4-31G level. Energies relative to R/kcal mol^{-1} are given in parentheses.

Compound	R	TS	P
I	−187.818 633 (0.0)	−187.709 769 (68.31)	−187.841 622 (−14.43)
II	−286.568 716 (0.0)	−286.438 246 (81.87)	−286.545 988 (14.26)
III	−385.301 322 (0.0)	−385.171 117 (81.70)	−385.284 548 (10.53)
IV	−484.036 028 (0.0)	−483.912 539 (77.49)	−484.008 469 (17.29)
V	−242.780 972 (0.0)	−242.645 896 (84.76)	−242.772 491 (5.32)
VI	−390.957 593 (0.0)	−390.847 390 (69.15)	−390.949 569 (5.03)

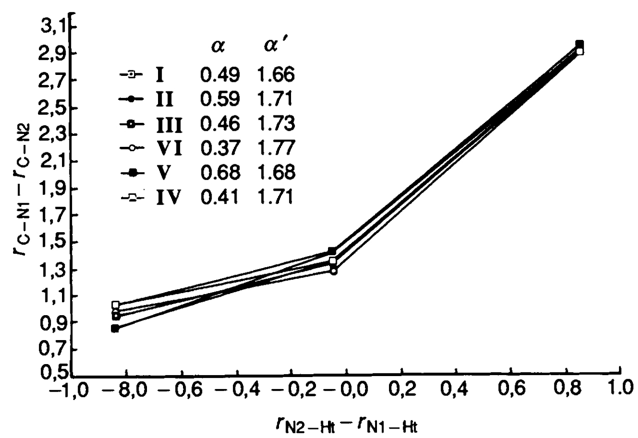

Fig. 2 Modified More O'Ferrall–Jencks diagram for the decomposition reactions of compounds **I–VI**. The difference in bond orders between C–N1 and C–N2 (r_{C-N1}–r_{C-N2}) *versus* the difference of bond orders between N2–Ht and N1–Ht (r_{N2-Ht}–r_{N1-Ht}) are represented. Values α and α′ are the slopes of the lines connecting R–TS and TS–P, respectively.

respectively, are equal. On the other hand the ordinates (r_{C-N1}–r_{C-N2}) change remarkably indicating that only the C–N1 and C–N2 bonds, respectively, are influenced.

The reaction path R–TS and TS–P is described by the slopes α and α′. For the fluoro-analogues **II–IV** the value of α decreases along the family. The value of α′ is almost constant at *ca.* 1.7. The treatment of this diagram predicts that a given perturbation of the transition state should produce a displacement parallel to the diagonal or perpendicular to it. The amount and direction of movement depends on structural and electronic features which can change the energies of R, P and the corners. It can be considered as an application of the perpendicular or parallel effects to the reaction profile elaborated by Thornton.[22] Substituent effects perpendicular to the reaction pathway, named 'anti-Hammond' effects, lead to the TS resembling more closely the species which has been stabilized. Thus, the stabilization of a point X out of the reaction pathway will lead to a new reaction pathway in which the TS has been shifted toward the point of stabilization. For this reaction, stabilization of a carbocation intermediate (upper left in Fig. 2) will lead to a TS with more carbocation character (*i.e.* **V**): the perpendicular effect is then larger than the parallel effect and the Hammond postulate is not then fulfilled, *i.e.* the location of TS does not move towards P and is not thus influenced by an increasing difference of enthalpy of the process. On the other hand, the principle of bond-order conservation is valid, *i.e.* the assumption that along the minimum-energy path the sum of bond orders of the forming (N2–Ht and C–N1) and breaking bonds (N1–Ht and C–N2) is constant.

The results for reactions of compounds **I–VI** show that the variation of the activation barrier value obtained from energetics does not necessarily reflect the real variation in the TS structure. In other words, it is not always correct to draw a conclusion on the variation in the transition-state structure from the variation of barrier height.

The results of the present study can be summarized as follows. (i) The electron-donating groups, as **V**, advance the TS position along the reaction path while the opposite effect is produced when an electron-withdrawing group is used. (ii) The curvature of the potential energy surface for the TS region and the components of the transition vectors are almost constant for all substituents. (iii) The barrier height and the structure of TS do not correlate with the reaction energy. (iv) The differences in the structure of TS with different substituents are consistent with the predictions based on a modified version of the More O'Ferral–Jencks type diagram. (v) The perpendicular effect is larger than the parallel effect; this fact is an example of the 'anti-Hammond' effect.

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References

1 M. J. Adams, M. Buehner, K. Chandrasekhar, G. C. Ford, M. L. Hackert, A. Liljas, M. G. Rossmann, I. E. Smiley, W. S. Allison, J. Everse, N. O. Kaplan and S. S. Taylor, *Proc. Natl. Acad. Sci. USA*, 1973, **70**, 1968.
2 J. F. Riordan, *Mol. Cell. Biochem.*, 1979, **26**, 71; S. Smrckova, *Chem. Listy*, 1988, **82**, 337.
3 J. Krechl, S. Smrckova, F. Pavlikova and J. Kuthan, *Collect. Czech. Chem. Commun.*, 1989, **54**, 2415; J. Krechl, S. Smrckova and J. Kuthan, *Collect. Czech. Chem. Commun.*, 1990, **55**, 460; J. Krechl, S. Smrckova, M. Ludwig and J. Kuthan, *Collect. Czech. Chem. Commun.*, 1990, **55**, 469; J. Krechl, S. Bohm, S. Smrckova and J. Kuthan, *Collect. Czech. Chem. Commun.*, in press.
4 B. Kratochvil, J. Ondracek, J. Krechl and J. Hasek, *Acta Crystallogr., Sect. C*, 1987, **43**, 2182; B. Kratochvil, J. Novotny, S. Smrckova and J. Krechl, *Collect. Czech. Chem. Commun.*, in press.
5 J. A. Gautier, M. Miocque and C. C. Farnoux, *The Chemistry of Amidines and Imidiates*, ed. S. Patai, Wiley, London, 1975; P. C. Schaefer, *The Chemistry of the Cyano Group*, ed. Z. Rappoport, Wiley, London, 1977.
6 J. Baker, M. Jones and M. Kilner, *Org. Mass. Spectrom.*, 1985, **20**, 619.
7 J. Andrés, J. Krechl, M. Carda and E. Silla, *Int. J. Quantum Chem.*, 1991, in press.
8 J. Andrés, J. Krechl and E. Silla, *Chem. Phys. Lett.*, 1990, **169**, 509.
9 I. H. Williams, D. Spangler, D. A. Femec, G. M. Maggiora and R. L. Schowen, *J. Am. Chem. Soc.*, 1980, **102**, 6621; I. H. Williams, G. M. Maggiora and R. L. Schowen, *J. Am. Chem. Soc.*, 1978, **100**, 747; T. H. Yamataka, S. Nagase, T. Ando and T. Hanafusa, *J. Am. Chem. Soc.*, 1986, **108**, 601; D. Spangler, I. H. Williams and M. G. Maggiora, *J. Comput. Chem.*, 1983, **4**, 524.
10 L. Schafer, *J. Mol. Struct., THEOCHEM*, 1983, **100**, 1; W. J. Hehre, L. Radom, P. R. von Schleyer and J. A. Pople, *Ab Initio Molecular Orbital Theory*, Wiley-Interscience, New York, 1986.
11 H. B. Schlegel, *J. Comput. Chem.*, 1982, **3**, 214; H. B. Schlegel, *Adv. Chem. Phys.*, 1987, **67**, 249; S. Bell and J. S. Grighton, *J. Chem. Phys.*, 1984, **80**, 2464; J. Baker, *J. Comput. Chem.*, 1986, **7**, 385; J. D. Head, B. Weiner and M. C. Zerner, *Int. J. Quantum Chem.*, 1988, **33**, 177.
12 M. R. Peterson and R. A. Poirier, Program MONSTERGAUSS, University of Toronto, 1983; W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton and J. A. Pople, GAUSSIAN 70, QCPE No. 236.
13 H. B. Schlegel, program FORCE, Ph.D. Thesis, Queen's University, Kingston, Canada, 1975.

14 N. C. Davidson, *Math. Prog.*, 1975, **9**, 1; S. Bell, J. Crighton and R. Fletcher, *Chem. Phys. Lett.*, 1981, **82**, 122.

15 M. J. D. Powell, VA05 program, Harwell Subroutine Library, Atomic Energy Research Establishment, Harwell, UK.

16 O. Tapia and J. Andrés, *Chem. Phys. Lett.*, 1984, **109**, 471.

17 G. S. Hammond, *J. Am. Chem. Soc.*, 1955, **77**, 334.

18 A. J. C. Varandas and S. J. F. Formosinho, *J. Chem. Soc., Faraday Trans. 2*, 1986, 282.

19 G. Lendvay, *J. Mol. Struct., THEOCHEM*, 1988, **167**, 331; G. Lendvay, *J. Phys. Chem.*, 1989, **93**, 4422.

20 R. A. More O'Ferrall, *J. Chem. Soc. B*, 1970, 274; W. P. Jencks, *Chem. Rev.*, 1972, **72**, 705; W. P. Jencks, *Acc. Chem. Res.*, 1980, **13**, 161.

21 I. Mayer, *Chem. Phys. Lett.*, 1983, **97**, 270.

22 E. R. Thornton, *J. Am. Chem. Soc.*, 1967, **89**, 2915.

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