CONFIGURATION ON THE C=N DOUBLE BOND OF MONOSUBSTITUTED AMIDINES AND AMIDOXIMES

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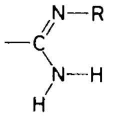
Received March 2, 1989
Accepted March 31, 1989

Configuration on the C=N double bond of amidines and amidoximes is controlled by steric effects on the second nitrogen atom but there is a difference in the case of N'-monosubstituted derivatives: amidines prefer *E* configuration (conformation around the C–N bond *sp*) and amidoximes *Z* configuration (conformation *ap*). This was confirmed by the X-ray structures of two analogous model compounds N,N'-dimethyl-4-nitrobenzamidine (monoclinic, $P2_1/c$, $a = 10{\cdot}855(3)$, $b = 11{\cdot}043(3)$, $c = 8{\cdot}593(3)$ Å, $\beta = 105{\cdot}69(2)°$, $V = 991{\cdot}8(5)$ Å^3, $Z = 4$, $D_x = 1{\cdot}29$ g cm^{-3}, CuK$_\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 7{\cdot}91$ cm^{-1}, $F(000) = 408$, $T = 291$ K, $R = 0{\cdot}065$ for 1 265 observed reflections) and N'-methyl-4-nitrobenzamidoxime (monoclinic, $P2_1/a$, $a = 6{\cdot}699(2)$, $b = 24{\cdot}178(9)$, $c = 6{\cdot}075(2)$ Å, $\beta = 106{\cdot}20(3)°$, $V = 944{\cdot}9(6)$ Å^3, $Z = 4$, $D_x = 1{\cdot}37$ g cm^{-3}, CuK$_\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 9{\cdot}22$ cm^{-1}, $F(000) = 408$, $T = 291$ K, $R = 0{\cdot}079$ for 1 278 observed reflections).

Configuration on the C=N bond of amidines is not yet always known with certainty since in many cases it must be investigated together with the conformation on the C—N bond and with the prototropic equilibrium. In a previous paper[1] we tried to develop some general rules according to which the configuration is controlled by steric requirements of substituents on the second nitrogen atom. In the case of derivatives with a free NH_2 group the *Z* configuration (*IZ*) is preferred as evidenced mainly by several X-ray structures[2-4]. In the case of N',N'-disubstituted derivatives the configuration is reversed as confirmed by numerous X-ray structures (reviewed in refs[1,5]) and by NMR studies in solution[1,6]. Even when the isomer *IIIZ* was isolated[7,8], it was less stable than *III E*. Similar regularity was found earlier for amidoximes[9,10]. The preferred configurations *IVZ* and *VI E* were found in solution from dipole moments[9,10] and in numerous crystal studies, see[11-16] and the work cited in ref.[9].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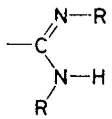
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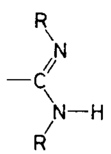
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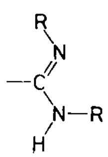
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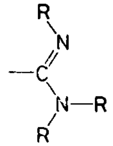
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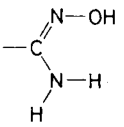
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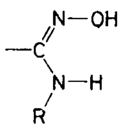
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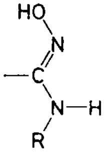
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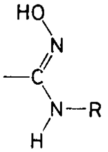
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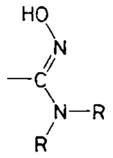
VI E

This report is concerned with N'-monoalkyl derivatives, *II* and *V*, the steric arrangement of which seems to be remarkably different. With two planar conformations around the partial double bond C—N' there are four possible conformers. If we disregard the sterically most crowded form *Zsp*, there remain still three forms *Zap*, *Eap*, *Esp*. In the crystalline state all amidines investigated were in the configuration *E*, twice[17,18] in the *II Esp*, once[5] in the *II Eap* form (not considering amidinium salts and zwitterions). Amidoximes were found always in the *V Zap* form, both in the crystal [19-21] and in solution[22]. We suggested[1] that the configuration is not controlled only by purely steric effects, however, an intramolecular hydrogen bond was not proven[9] in the compounds of the type *IV Z*. The above examples of crystal structures[5,17-21] are quite unsystematic, those of amidines and amidoximes are not comparable. Therefore, we prepared two similar model compounds, N,N'-dimethyl-4-nitrobenzamidine (*IIa* – Fig. 1) and N'-methyl-4-nitrobenzamidoxime (*Va*), and determined their X-ray structures.

EXPERIMENTAL

N,N'-*Dimethyl-4-nitrobenzamidine* (IIa). N-Methyl-4-nitrobenzamide was heated with PCl_5 (130 mole %) to 100°C for 4 hours, $POCl_3$ distilled off and N-methyl-4-nitrobenzimidoyl chloride distilled at reduced pressure, b.p. 166°C/1·9 kPa. Benzimidoyl chloride was immediately reacted with an excess of methylamine in toluene solution, methylamine hydrochloride was filtered off, and the filtrate evaporated, yield 60%, m.p. 152°C (benzene–cyclohexane), ref.[23] gives 149°C for a sample prepared in another way. For $C_9H_{11}N_3O_2$ (193·2) calculated: 55·98% C, 5·74% H, 21·75% N; found: 56·01% C, 5·72% H, 22·12% N. Crystals were obtained by evaporation from benzene: for X-ray analysis a parallelepiped crystal with dimensions 0·21 × 0·18 × 0·10 mm was taken. Lattice parameters were refined using 20 reflections in the range $5° \leq 2\Theta \leq 30°$. 1 788 $h, k, \pm l$ independent reflections with $\sin \Theta/\lambda \leq 0{\cdot}60$ Å^{-1}; $0 \leq h \leq 12$, $0 \leq k \leq 12$, $-10 \leq l \leq 9$, 1 265 with $I \geq 2{\cdot}5\sigma(I)$; $w = 1/(\sigma^2 + 0{\cdot}00051F^2)$, $R = 0{\cdot}065$, $R_w = 0{\cdot}073$ for

1 265 observed reflections; final maximum shift to error 0·04; $S = 2·77$; maximum and minimum heights in final difference Fourier synthesis 0·21 and $-0·23$ e Å^{-3}.

N'-*Methyl-4-nitrobenzamidoxime* (Va). 4-Nitrobenzohydroximoyl chloride in dry ether was added to a solution of methylamine in toluene (in excess) at a temperature below 0°C, stirring was continued for 3 hours and temperature increased to 20°C. Methylamine hydrochloride was

TABLE I

Atomic coordinates (.10^4) and equivalent temperature factors Å^2 for compounds *IIa* and *Va*

Atom	x/a	y/b	z/c	B_{eq}^{a}
		Compound *IIa*		
C(1)	2 260(3)	9 288(3)	−529(4)	4·50(5)
C(2)	1 826(3)	10 439(3)	−981(4)	5·22(7)
C(3)	2 430(4)	11 147(3)	−1 857(5)	5·91(7)
C(4)	3 470(3)	10 679(3)	−2 280(4)	5·63(7)
C(5)	3 924(4)	9 542(4)	−1 822(5)	6·26(8)
C(6)	3 306(3)	8 832(3)	−957(4)	5·20(6)
C(7)	1 577(3)	8 524(3)	455(4)	4·45(5)
N(8)	1 441(3)	8 765(2)	1 818(3)	5·07(5)
C(9)	2 018(5)	9 866(4)	2 693(6)	6·83(9)
N(10)	1 033(3)	7 524(3)	−366(4)	5·62(6)
C(11)	338(4)	6 666(3)	319(5)	5·88(7)
N(12)	4 109(4)	11 442(4)	−3 217(5)	7·73(8)
O(13)	5 052(5)	11 072(4)	−3 496(7)	13·99(14)
O(14)	3 685(4)	12 416(4)	−3 641(6)	11·80(11)
		Compound *Va*		
C(1)	9 547(4)	6 082(1)	4 050(4)	5·78(5)
C(2)	9 838(5)	6 602(1)	3 242(5)	6·83(6)
C(3)	11 085(5)	6 982(1)	4 708(6)	7·24(6)
C(4)	12 022(4)	6 824(1)	6 939(5)	7·15(6)
C(5)	11 822(5)	6 309(2)	7 720(5)	7·70(6)
C(6)	10 539(5)	5 933(1)	6 257(5)	7·19(6)
C(7)	8 193(4)	5 677(1)	2 528(4)	5·80(4)
N(8)	9 010(3)	5 421(1)	1 110(4)	6·31(4)
O(9)	7 550(3)	5 039(1)	−285(3)	6·93(4)
N(10)	6 276(4)	5 583(1)	2 703(5)	8·24(6)
C(11)	5 350(6)	5 862(2)	4 290(7)	8·85(8)
N(12)	13 232(5)	7 234(2)	8 524(6)	9·11(8)
O(13)	13 126(5)	7 714(1)	7 972(6)	11·48(8)
O(14)	14 329(5)	7 067(2)	10 411(6)	12·32(8)

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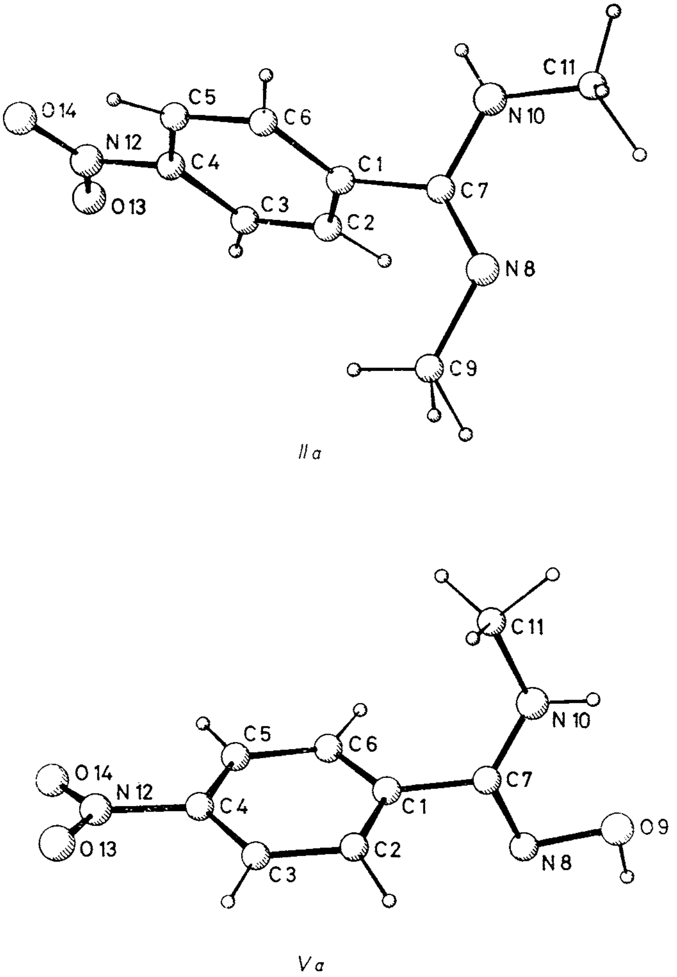
[a] $B_{eq} = (8/3)\,\pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$.

filtered off and the filtrate evaporated, yield 82%, m.p. 178°C (decomp., toluene). For $C_8H_9N_3O_3$ (195·2) calculated: 49·24% C, 4·65% H, 21·53% N; found: 49·19% C, 4·62% H, 21·42% N. Crystals were obtained by slow cooling of a solution in acetone–hexane (1 : 3): parallelepiped crystal with dimensions 0·40 × 0·30 × 0·05 mm. Lattice parameters were refined using 14 reflections in the range $5° \leqq 2\Theta \leqq 50°$. 1 695 $h, k, \pm l$ independent reflections with $\sin \Theta/\lambda \leqq 0·60$ Å^{-1}; $0 \leqq h \leqq \leqq 8$, $0 \leqq k \leqq 28$, $-7 \leqq l \leqq 6$, 1 278 with $I \geqq 2·5\sigma(I)$; $w = 1/(\sigma^2 + 0·01692F^2)$, $R = 0·079$, $R_w = 0·093$ for 1 278 observed reflections (poor quality of the crystals); final maximum shift to error $0·06S = 0·95$; maximum and minimum heights in final difference Fourier synthesis 0·17 and −0·29 e Å^{-3}.



IIa

Va

FIG. 1

View of the molecules of N,N′-dimethyl-4-nitrobenzamidine (*IIa*) and N′-methyl-4-nitrobenzamidoxime (*Va*) showing also the atom numbering (program PLUTO (ref.[27]))

For both *IIa* and *Va* a Huber four circle diffractometer was used, graphite monochromatized CuK$_\alpha$ radiation; standard reflection checked every 50 reflections: no significant deviation. Structure was solved by SHELXS-86 (ref.[24]), all H atoms from difference Fourier synthesis; anisotropic least-squares refinement (SHELX-76 (ref.[25])) using F; H isotropic with a common refined temperature factor; atomic scattering factors taken from international tables[26].

RESULTS AND DISCUSSION

The atomic parameters are given in Table I for the compounds *IIa* and *Va*. Figure 1 shows the two molecules and numbering of atoms. Bond distances and angles are collected in Tables II and III, torsion angles in Table IV.

TABLE II
Bond distances (Å) in compounds *IIa* and *Va*

Bond	*IIa*	*Va*	Bond	*IIa*	*Va*
C(1)—C(2)	1·375(4)	1·382(4)	N(8)—C(9)	1·478(5)	—
C(2)—C(3)	1·369(5)	1·385(4)	N(8)—O(9)	—	1·438(3)
C(3)—C(4)	1·377(5)	1·379(4)	C(7)—N(10)	1·356(4)	1·337(3)
C(4)—C(5)	1·367(5)	1·352(5)	N(10)—C(11)	1·432(4)	1·450(4)
C(5)—C(6)	1·375(5)	1·389(5)	C(4)—N(12)	1·463(5)	1·460(4)
C(6)—C(1)	1·380(4)	1·369(3)	N(12)—O(13)	1·185(5)	1·203(5)
C(1)—C(7)	1·521(4)	1·473(3)	N(12)—O(14)	1·189(5)	1·243(4)
C(7)—N(8)	1·249(4)	1·299(3)			

TABLE III
Bond angles (in °) in compounds *IIa* and *Va*

Angle	*IIa*	*Va*	Angle	*IIa*	*Va*
C(1)—C(2)—C(3)	120·3(3)	119·6(2)	N(8)—C(7)—N(10)	121·0(3)	124·3(2)
C(2)—C(3)—C(4)	118·7(3)	118·5(3)	C(7)—N(8)—C(9)	120·8(3)	—
C(3)—C(4)—C(5)	121·8(3)	122·5(2)	C(7)—N(8)—O(9)	—	110·7(2)
C(4)—C(5)—C(6)	119·3(3)	118·9(3)	C(7)—N(10)—C(11)	121·9(3)	124·9(3)
C(5)—C(6)—C(1)	119·6(3)	119·9(3)	C(3)—C(4)—N(12)	118·3(4)	118·5(3)
C(6)—C(1)—C(2)	120·4(3)	120·7(3)	C(5)—C(4)—N(12)	119·9(4)	119·0(3)
C(2)—C(1)—C(7)	119·3(3)	120·3(2)	C(4)—N(12)—O(13)	118·5(4)	119·4(4)
C(6)—C(1)—C(7)	120·3(3)	119·0(2)	C(4)—N(12)—O(14)	119·2(4)	117·7(4)
C(1)—C(7)—N(8)	127·0(3)	115·7(2)	O(13)—N(12)—O(14)	122·3(4)	122·9(3)
C(1)—C(7)—N(10)	111·8(2)	120·0(2)			

The fundamental difference between the two structures is in the configuration, also the conformation around the C—N bond is opposite. This result confirms our observation[1] made on unsystematic literature data. Disubstituted amidines apparently prefer configuration *E*, either in the conformation *sp* or *ap*. The latter (*II Eap*) seems to be less frequent and restricted to derivatives with a very small substituent on C, maybe only to formamidines[5]. Formation of a dimer, similar to that of carboxylic acids, is not deciding for the conformational equilibrium and not sufficient to stabilize this form with respect to *Esp* in the case of compound *IIa* and of other derivatives[17,18]. In the crystal structure of *IIa* intermolecular hydrogen bonds of another type are present, connecting the atoms N(10) and N(8): N(10)···N(8*) = 2·942(5) Å, H(10)···N(8)* = 2·19(5) Å.

All monosubstituted amidoximes investigated till now are in the form *VZap*. A possible intramolecular hydrogen bond[9] is not evident from the structure of *Va*. Although the functional group is planar, the distance H(10)···O(9) of 2·22 Å seems to be too long to allow for a strong bond under the given, unfavourable steric conditions. According to provisional results of IR spectroscopy[28] a hydrogen bond is not clearly observable even in solution. In the crystal of *Va* hydrogen bonds of another type are present, forming a cyclic dimer on the oximino group: O(9)···N(8*) 2·728(5) Å, H(9)···N(8*) 1·84(4) Å.

We conclude that configurations of amidines and amidoximes and the differences between these two classes are controlled by rather subtle effects, essentially of steric origin. The steric hindrance is also evident from the widened angles C(1)—C(7)—

TABLE IV

Torsion angles (in °, *s* = 1) in compounds *IIa* and *Va*

Angle	*IIa*	*Va*	Angle	*IIa*	*Va*
C(1)—C(2)—C(3)—C(4)	0	0	C(1)—C(7)—N(8)—C(9)	−3	—
C(2)—C(3)—C(4)—C(5)	−1	2	C(1)—C(7)—N(8)—O(9)	—	180
C(3)—C(4)—C(5)—C(6)	2	−3	N(10)—C(7)—N(8)—C(9)	−179	—
C(4)—C(5)—C(6)—C(1)	−2	2	N(10)—C(7)—N(8)—O(9)	—	2
C(5)—C(6)—C(1)—C(2)	1	1	C(1)—C(7)—N(10)—C(11)	180	1
C(6)—C(1)—C(2)—C(3)	0	−2	N(8)—C(7)—N(10)—C(11)	−3	180
C(3)—C(2)—C(1)—C(7)	180	179	C(2)—C(3)—C(4)—N(12)	180	−176
C(5)—C(6)—C(1)—C(7)	−179	180	C(6)—C(5)—C(4)—N(12)	180	175
C(2)—C(1)—C(7)—N(8)	−60	79	C(3)—C(4)—N(12)—O(13)	175	11
C(6)—C(1)—C(7)—N(8)	119	−100	C(5)—C(4)—N(12)—O(13)	−3	−167
C(2)—C(1)—C(7)—N(10)	116	−103	C(3)—C(4)—N(12)—O(14)	−3	−169
C(6)—C(1)—C(7)—N(10)	−64	79	C(5)—C(4)—N(12)—O(14)	178	12

—N(8) in *IIa* and C(1)—C(7)—N(10) and C(7)—N(10)—C(11) in *Va* (Table III). According to the twist angles between the benzene ring and the plane of the functional group, this hindrance seems to be slightly stronger in the amidoxime molecule (80° as compared to 62° – Table IV). The planarity of the functional group is not disturbed. Of the other geometrical parameters the bond lengths C=N and C—N show significant differences (Table II): the functional group of amidoximes appears as more conjugated than in amidines. This fact is understandable in virtue of the enhanced acceptor ability of the imino nitrogen in the =NOH group; it is corroborated by the values of mesomeric dipole moments[1] but was not detected in a plot of all available C=N and C—N bond lengths[1] due to a large scatter. Of the remaining parameters, the extraordinary extended C(1)—C(7) bond in *IIa* (Table II) remains without explanation.

REFERENCES

1. Exner O., Buděšínský M., Hnyk D., Všetečka V., Raczyńska E. D.: J. Mol. Struct. *178*, 147 (1988).
2. Iwasaki F., Akiba K.-Y.: Acta Crystallogr., B *37*, 185 (1981).
3. Korbonits D., Kiss P., Simon K., Kolonits P.: Chem. Ber. *117*, 3183 (1984).
4. Norrestam R., Mertz S., Crossland I.: Acta Crystallogr., C *39*, 1554 (1983).
5. Anulewicz R., Krygowski T. M., Pniewska B.: J. Crystallogr. Spectrosc. Res. *17*, 661 (1987).
6. Oszczapowicz J., Raczyńska E., Osek J.: Magn. Reson. Chem. *24*, 9 (1986).
7. Hegarthy A. F., Chandler J.: J. Chem. Soc., Chem. Commun. *1980*, 130.
8. Hegarthy A. F., Chandler J.: Tetrahedron Lett. *1980*, 885.
9. Exner O., Motekov N.: Collect. Czech. Chem. Commun. *43*, 2740 (1978).
10. Exner O., Motekov N.: Collect. Czech. Chem. Commun. *47*, 814 (1982).
11. Solans X., Miravitlles C., Declercq J.-P., Germain G.: Acta Crystallogr., B *36*, 3121 (1980).
12. Tinant B., Declercq J.-P., Germain G., Van Meerssche M.: Bull. Soc. Chim. Belg. *90*, 1177 (1981).
13. Endres H., Kadkhodai-Elyaderani N.: Z. Naturforsch., B *37*, 1255 (1982).
14. Jeffrey A. G., Ruble J. R., McMullan R. K., Defrees D. J., Pople J. A.: Acta Crystallogr., B *37*, 1381 (1981).
15. Mishnev A. F., Bundule M. F., Bleidelis Ya. Ya., Andrianov V. G., Eremeev A. V.: Zh. Strukt. Khim. *25* (5), 117 (1984).
16. Endres H., Schendzielorz M.: Acta Crystallogr., C *40*, 453 (1984).
17. Korp J. D., Bernal I.: Chem. Scr. *22*, 60 (1983).
18. Declercq J.-P., Germain G., Van Meerssche M., Van den Bril M., Fuks R.: Cryst. Struct. Commun. *9*, 1011 (1980).
19. Gieren A., Dederer B.: Acta Crystallogr., B *33*, 3296 (1977).
20. Dondoni A.. Gilli G., Sacerdoti M.: J. Chem. Soc., Perkin Trans. 2, *1976*, 1036.
21. Miravitlles C., Solans X., Germain G., Declercq J.-P.: Cryst. Struct. Commun. *9*, 621 (1980).
22. Exner O., Jehlička V., Dondoni A., Boicelli A. C.: J. Chem. Soc., Perkin Trans. 2, *1974*, 567.
23. Piskov V. B., Kasperovich V. P.: Zh. Org. Khim. *14*, 820 (1978).
24. Sheldrick G. M. in: *Crystallographic Computing 3* (G. M. Sheldrick, C. Kruger and R. Goddard, Eds), p. 175. Oxford University Press, Oxford 1985.

25. Sheldrick G. M.: *SHELX76. Program for Crystal Structure Determination.* University of Cambridge 1976.
26. *International Tables for X-Ray Crystallography,* Vol. IV. Kynoch Press, Birmingham 1974.
27. Motherwell S., Clegg W.: *PLUTO.* University of Cambridge, Cambridge 1978.
28. Fiedler P., Exner O.: Unpublished results.