CONFIGURATION AND CONFORMATION OF N,N'-DIARYLAMIDINES: A DIPOLE MOMENT STUDY

Václav VŠETEČKA[a], Janusz OSZCZAPOWICZ[b] and Otto EXNER[c]

[a]*Department of Organic Chemistry,*
Charles University, 128 40 Prague 2, Czechoslovakia
[b]*Chemistry Department,*
University of Warszaw, 01093 Warszaw, Poland
[c]*Institute of Organic Chemistry and Biochemistry,*
Czechoslovak Academy of Sciences, 166 10 Prague 6, Czechoslovakia

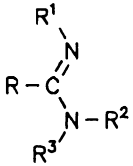
Received May 4, 1992
Accepted June 30, 1992

Dedicated to Professor Václav Horák on the occasion of his 70th birthday.

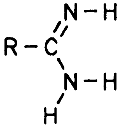
Dipole moments of N,N'-diphenylformamidine and its *para*-halogen derivatives were measured in benzene solution. Since the prototropic rearrangement is degenerate, the dipole moments can be simply interpreted in terms of the *E* configuration on C=N and a conformational equilibrium on C–N. The two forms, *Eap* and *Esp*, are populated approximately in the 1 : 1 ratio: the former is the conformation found in the crystal. The dipole moments anticipated for individual conformations were calculated by vector addition of bond moments: the previously determined correction for conjugation was found unnecessary.

Steric arrangement of amidines depends rather sensitively on substitution and this dependence is not yet fully understood[1 – 3].

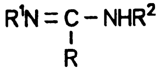
In the case of N,N',N'-trisubstituted derivatives (*I*) the *E* configuratinon was found in crystal (see e.g. refs[4 – 7]) as well as in solution[2]; one important exception was observed[8] with R = t-butyl. Amidines *II* with an unsubstituted NH_2 group take the *Z* configuration but the evidence is somewhat scarce[9,10] since in some cases the configuration might be affected by an intramolecular hydrogen bond[11,12]. With this exception all the observations may be easily explained by steric effects of the substituents.



I



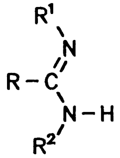
II



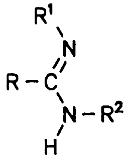
$$R^1N=\underset{\displaystyle R}{\underset{|}{C}}-NHR^2$$

III, R = C_6H_5; R^1 = R^2 = CH_3
IV, R = 4-$NO_2C_6H_4$; R^1 = R^2 = CH_3
V, R = R^1 = R^2 = C_6H_5
VI, R = CH_3, R^1 = R^2 = 4-$CH_3C_6H_4$
VII, R = H; R^1 = R^2 = C_6H_5
VIII, R = H; R^1 = R^2 = 4-ClC_6H_4
IX, R = H; R^1 = R^2 = 4-BrC_6H_4

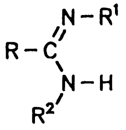
In the case of N,N′-bisderivatives (*III* – *IX*) the problem is more complex. In addition to the configuration on C=N one has to determine the conformation on the partially double bond C–N. Alltogether four planar forms are to be considered, *Eap*, *Esp*, *Zap*, *Zsp*, the last of which is sterically overcrowded and hence practically excluded.



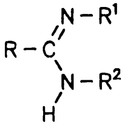
Eap



Esp



Zap



Zsp

On several derivatives different results were obtained. N,N′-Dimethyl-4-nitrobenzamidine (*IV*) is in the form *Esp* in crystal[3] and this form prevails even in solution[13] for compounds *III* and *IV*. The same solid-state conformations was found[14,15] with the N,N′-diaryl derivatives *V*, *VI* and with two sterically overcrowded amidines[16,17] which are not quite typical. On the other hand, N,N′-diphenylformamidine (*VII*) in crystal[18] is in the *Eap* form which is stabilized by intermolecular hydrogen bonds forming a symmetrical dimer[19,20]. In solution an equilibrium was observed at low temperatures[19] ascribed to conformers *Eap* and *Esp*. Since the hydrogen bonding would be possible even in compounds *III* and *IV*, it is probably of importance mainly for the solid-phase conformation. If even the conformation of isolated molecules *III* and *VII* is actually different, it could be attributed to different steric requirements of R = H as compared to R = phenyl.

The object of the present communication is to determine this conformation in benzene solution from dipole moments. The results are to be compared with low-temperature NMR spectroscopy[19] and with an IR study carried out simultaneously[21]. These methods are complementary to a certain degree. While the dipole moment approach is less sensitive to the presence of minor forms, a misassignment is easier to do in spectroscopic methods. In a previous study[2] the configuration of trisubstituted amidines was known and the dipole moments were used to evaluate the extent of conjugation. On the contrary the problem in this study is to determine the steric arrangement while the extent of conjugation can be estimated from previous results[2]. The compounds *VII* – *IX* were selected. The symmetrical substitution, $R^1 = R^2$, is necessary to avoid problems which might arise with a prototropic rearrangement when the position of equilibrium is not known. The *para* substituents, 4-Cl and 4-Br, in *VIII* and *IX* serve only to extend the amount of information: they allow the well-tried graphical representation[22] to be used. (Restriction to these compounds was dictated also by the low solubility of some others, particularly of N,N'-bis(4-nitrophenyl)formamidine.) There is a basic assumption that remote substituents do not affect the conformation[23].

EXPERIMENTAL

The compounds *VII* – *IX* were described[24]. Determination of dipole moments in benzene was carried out as previously[2], using the method of Halverstadt and Kumler[25]. The experimental data are listed in Table I together with the molar refractions (calculated from increments[26]) and resulting dipole moments (calculated with a 5% correction for atomic polarization).

Dipole moments expected for the individual conformations were calculated by vector addition of standard bond moments[27] (in Debyes*, direction from the positive toward the negative end): H–C(al) 0.3, H–C(ar) 0, C=N 1.8, C–N 0.45, H–N 1.3, C(ar)–Cl 1.6, C(ar)–Br 1.57. No correction was applied for the conjugation N-aryl, assuming that the benzene rings are not coplanar, see ref.[28]. For a possible correction for the conjugation within the amidine grouping see Results and Discussion. The bond angles were taken from the X-ray structure[18] of *VII*: the angles on N deviate only insignificantly from 120°.

RESULTS AND DISCUSSION

Stereochemical studies of amidines can be complicated by prototropic rearrangement (tautomerism) and/or conjugation within the functional group: the latter problem arises particularly when dipole moments are used as the experimental tool. In the case of our compounds an additional problem may be formation of dimers in solution[19,20,29]. We shall discuss these problems in turn.

Dimerization in solution could depreciate the results considerably, in particular when the dimer is symmetrical and has zero dipole moment. It is true that standard methods[25]

---

* 1 D (Debye) = $3.336 \cdot 10^{-30}$ C m.

evaluate the dipole moment from an extrapolation to zero concentration, but this procedure need not be reliable[30] when the equilibrium constant K is large. Its two experimental values given in the literature[20,31] for compound *VII* are widely apart, $K = 69$ and 19 kg mol^{-1}, respectively: both were determined cryoscopically at 5 °C. Our permittivity measurements at 25 °C reveal much less dimer formation. In Fig. 1 the permittivity ε is plotted vs the weight fraction w_2 for compound *IX* for which there was the largest deviation from linearity. The straight line drawn through the first three points gives a reliable value of the slope at zero concentration (denoted α) and hence also of the dipole moment of the monomer. The two points at higher concentrations deviate in the expected direction and prove some dimer formation. However, the equi-

TABLE I

Dipole moment data (in benzene) of N,N'-diarylamidines *VII* – *IX*

Parameter	*VII*	*VIII*	*IX*
para Substituent	H	Cl	Br
α^a	2.183	4.225	3.029
β^a	-0.216	-0.311	-0.342
P_2^0, cm^3 mol^{-1}	134.9	276.9	286.6
$R_D{}^b$, cm^3 mol^{-1}	63.8	73.4	79.2
$\mu_{exp}{}^c$, D	1.83	3.13	3.16
μ_{calc}, D (*Eap*)	1.32 (2.19)^d	1.67 (2.40)^d	1.65 (2.39)^d
(*Esp*)	2.65 (3.38)^d	4.17 (4.91)^d	4.14 (4.88)^d
(*Zap*)	1.60 (2.49)^d	0.64 (1.30)^d	0.64 (1.31)^d

[a] Slopes of the plots ε_{12} vs w_2 and d_{12}^{-1} vs w_2, respectively; [b] with a 5% correction for atomic polarization; [c] calculated from increments; [d] in parentheses, calculated with a correction for the n–π conjugation, see Results and Discussion.

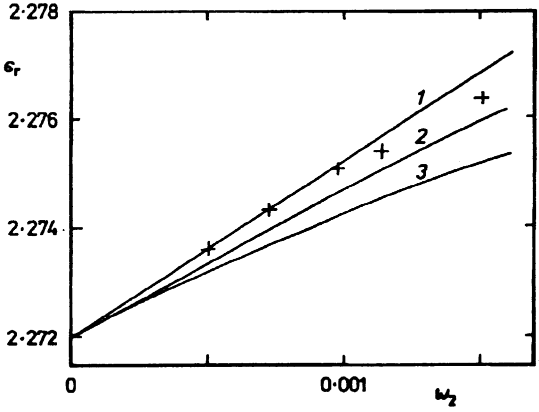


FIG. 1

The Halverstadt–Kumler plot of the relative permittivity ε_{12} of the solution vs the weight fraction w_2 of the solute *IX*. Straight line *1* tangent at $w_2 \to 0$ from which the dipole moment of the monomer was calculated; curve *2* calculated for $K = 19$; curve *3* calculated for $K = 69$ (kg mol^{-1})

librium constant cannot be as large as reported[20,31] for compound *VII*, as seen from the calculated curves. With respect to the statistical problems[30] we cannot estimate K from our data but it must be rather less than the lower value from the literature[31]: the main reason is evidently the dependence on temperature. For compound *VIII* the deviation from linearity is still less, and for *VII* no deviation was observed. We conclude that at the concentrations used in our work, the dipole moment of the monomeric form can be determined with a usual precision.

A prototropic rearrangement in our compounds was proven by both ^{1}H and ^{13}C NMR spectroscopy: compound *VII* shows[19] a single signal ^{1}H(N), all compounds *VII* – *IX* give single signals[32] for all aromatic ^{13}C. Similar observations were made with other N,N'-disubstituted amidines[29], unless the temperature was lowered[19] to 180 K. Whereas the exchange of proton is fast in the NMR time scale, it can be still regarded as slow in the time scale of dipole moments, i.e. compared to the rate of orientation of molecules.

For a slow equilibrium of several forms the effective dipole moment is given[33] by Eq. (*1*)*. In the case of compounds *VIII* – *IX* the rearrangement is degenerate: the populations N_i are equal and the effective dipole moment equals that of the single form.

$$\mu_{ef}^2 = \sum_{i=1}^{n} N_i \, \mu_i^2 \qquad (1)$$

Conjugation within the functional group (an n–π conjugation) is evidenced by the small difference between the C=N and C–N bond lengths in *VII* (131.1 and 132.3 pm, respectively[18]), also by the angles C=N–C and C–N–C which both are almost equal[18] to 120°. The difference in bond lengths is very small even when compared to other amidines[2,18]: this is at least partly due to the formation of a symmetrical dimer[18]. Any information from the gas phase measurements is not available.

The effect of mesomerism on dipole moments is expressed[34,35] by Eq. (*2*) since the mesomeric "rearrangement" is imagined as a process faster than any chemical or physical change.

$$\vec{\mu}_{ef} = (1-p)\,\vec{\mu}_{cl} + p\,\vec{\mu}_{pol} \qquad (2)$$

The contribution of the polar formula, p, could be in principle calculated from this equation[35], but it is difficult to estimate reliably its pertinent dipole moment $\vec{\mu}_{pol}$. We have always preferred[2,36] to calculate only the dipole moment of the nonpolar formula, $\vec{\mu}_{cl}$ and to express the experimental result in the form of the so-called mesomeric dipole moment, $\vec{\mu}_m$, according to Eq. (*3*).

---

* Ref.[33] states that Eq. (*1*) is valid for both slow and rapid equilibria. This is true assuming that all actual chemical reactions are slower than the orientation of molecules (~ 10^{-11} s).

$$\vec{\mu}_m = \vec{\mu}_{exp} - \vec{\mu}_{cl} \qquad (3)$$

Defined in this way, $\vec{\mu}_m$ appears as an empirical improvement to the bond moment scheme when the actual dipole moment is to be predicted only on the basis of the classical nonpolar formula. The value of μ_m was estimated by us[2] for trisubstituted amidines *I* of two types: with R = C_6H_5, $R^1 = R^2 = R^3 = CH_3$ (μ_m = 0.88 D) and with R = H, $R^1 = C_6H_5$, $R^2 = R^3 = CH_3$ (μ_m = 1.81 D). The values of μ_m thus depend significantly on substitution: generally for a group X=C–Y they increase[2,36] with both the acceptor ability of X and donor ability of Y. For compounds *VII* – *IX* μ_m is expected significantly smaller than 0.88 D but it need not be much greater than zero. We left the decision to a posteriori arguments. Two sets of predicted values were calculated: one with μ_m = 0.9 D, the other with μ_m = 0. Comparison with experimental results revealed that only small values of μ_m are acceptable whatever the steric arrangement of the molecule may be: the best value of μ_m was just near to zero.

It was proven that dimerization and prototropic rearrangement do not affect the measured dipole moment at all, while the effect of conjugation may be treated as a provisionally unknown parameter. With these presumptions we may attempt to determine configuration and conformation according to the standard method[22]. When we take into account simultaneous occurence of three forms, *Eap*, *Esp*, *Zap*, Eq. (*1*) has three terms and two unknowns (since $N_1 + N_2 + N_3 = 1$). When the conformational equilibrium does not depend on substitution, three equations can be written for compounds *VII* – *IX*. However, for *VIII* and *IX* the equations are practically identical and even the remaining two equations for two unknowns may be numerically unstable. Better insight may be gained from the graphical representation[22]. In Fig. 2 are plotted quadrats of dipole moments, on the x-axis for the unsubstituted compound *VII*, on the y-axis for the dichloro derivative *VIII*: the dibromo derivative *IX* would yield the same picture. The experimental point (shadowed in Fig. 2) is situated near to the tie line of the points for the forms, *Eap* and *Esp*. This can be interpreted in two ways: either as a mixture of these conformers, approximately in the ratio 1 : 1, or as a nonplanar conformation with a torsion angle on the C–N bond approximately 90°. Only the first possibility is acceptable with respect to the mentioned double bond character of the C–N bond. The accuracy of the whole approach must not be overestimated: the shadowed circle in Fig. 2 is a rough estimate not only of the experimental error but also of the accuracy of the bond moment scheme used in the calculations. There is no evidence for the existence of the *Zap* form, although its presence in several percents cannot be excluded. The result is acceptable since *Eap* is the conformation of *VII* in the crystalline phase[18]. Note also that no agreement with experimental data can be obtained when a mesomeric correction[2] for the conjugation N=C–N is applied: in a graphical representation analogous to Fig. 2 (not shown) the experimental point would be situated far outside the calculated values.

Our results can be compared to those of a ^1H and ^{19}F NMR study[19] of *VII* and its 4,4'-difluoro derivative, and of an IR study[21] of *VII* and *VIII*, both carried out in different solvents, one also at a much lower temperature[19]. The position of the conformational equilibrium was not equal for individual compounds[19,21] while our approach works only with the assumption that *para* substitution does not affect conformational equilibrium[23]. If the assumption does not hold exactly, the experimental point in Fig. 2 would deviate from the calculated straight line. From the NMR and IR data[19,21] we can calculate the points shown in Fig. 2. The agreement with our results is not so bad, considering the differences in the conditions and even structure, also the well known objection that the band intensities of two isomers need not be equal. We may say that dipole moments have confirmed the spectral findings under different conditions, the merit of dipole moments being particularly the unambiguous assignment.

In conclusion we may comment the apparent discrepancy between different conformations of the compounds[3] *III* and *IV* on the one hand and *VII* – *IX* on the other[18]. All the compounds exist in solution as mixtures of the conformers *Eap* and *Esp*, approximately in a ratio not very far from 50% (refs[13,21] and this work). When they crystallize from the solution, *IV* prefers[3] conformation *Esp* and *VII Eap* (ref.[18]): the difference is evidently due to packing forces. The example shows that conformation of amidines is rather variable and sensitive to small substituent effects, particularly in the crystalline phase. The configuration on C=N is more rigid and more regular: it can be understood in terms of steric effects as outlined in the introduction. This example shows also the limitations of the dipole moment approach when assigning conformation and configuration, note several assumptions and simplification which were stated here clearly. In fact the reliability of the results depends very often on their concordance for various derivatives and various classes of compounds.

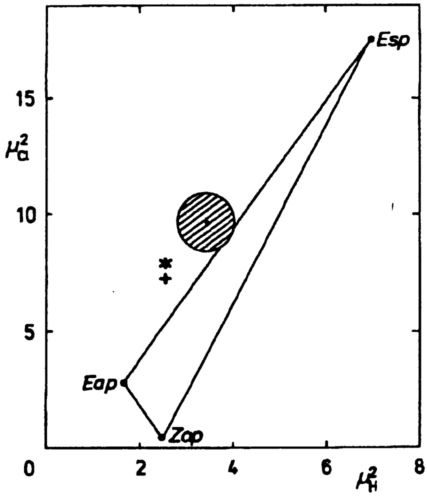


Fig. 2

Plot of the squared dipole moments of *VII* (*x*-axis) and *VIII* (*y*-axis), experimental (hatched circle) and calculated for individual conformations; * conformer population according to the IR results in carbon tetrachloride[21]; + conformer population according to the NMR results[19] (N,N'-bis(4-fluorophenyl)formamidine, tetrahydrofuran, 180 K)

REFERENCES

1. Häfelinger G. in: *The Chemistry of Amidines and Imidates* (S. Patai, Ed.), p. 1. Wiley, London 1975.
2. Exner O., Buděšínský M., Hnyk D., Všetečka V., Raczynska E. D.: J. Mol. Struct. *178*, 147 (1988).
3. Tinant B., Dupont-Feneau J., Declerq J.-P., Podlaha J., Exner O.: Collect. Czech. Chem. Commun. *54*, 3245 (1989).
4. Gilli G., Bertolasi V., Bellucci F., Ferretti V.: J. Am. Chem. Soc. *108*, 2420 (1986).
5. Krajewski J. W., Urbanczyk-Lipkowska Z., Gluzinski P., Busko-Oszczapowicz I., Bleidelis J., Kemme A.: Pol. J. Chem. *55*, 1015 (1981).
6. Tykarska E., Jaskólski M., Kosturkiewicz Z.: Acta Crystallogr., C *42*, 208 and 740 (1986).
7. Gifkins M. R., Jacobson R. A.: Cryst. Struct. Commun. *9*, 959 (1980).
8. Ciszak E., Gdaniec M., Jaskólski M., Kosturkiewicz Z., Owsianski J., Tykarska E.: Acta Crystallogr., C *45*, 433 (1989).
9. Norrestam R., Mertz S., Crossland I.: Acta Crystallogr., C *39*, 1554 (1983).
10. Surma K., Jaskólski M., Kosturkiewicz Z., Oszczapowicz J.: Acta Crystallogr., C *44*, 1031 (1988).
11. Iwasaki F., Akiba K.-Y.: Acta Crystallogr., B *37*, 185 (1981).
12. Korbonits D., Kiss P., Simon K., Kolonits P.: Chem. Ber. *117*, 3183 (1984).
13. Exner O., Jehlička V.: Unpublished results.
14. Alcock N. W., Barker J., Kilner M.: Acta Crystallogr., C *44*, 712 (1988).
15. Ciszak E., Gdaniec M., Jaskólski M., Kosturkiewicz Z.: Acta Crystallogr., C *44*, 2144 (1988).
16. Declerq J.-P., Germain G., Van Meerssche M., van den Bril M., Fuks R.: Cryst. Struct. Commun. *9*, 1011 (1980).
17. Korp J. D., Bernal I.: Chem. Scr. *22*, 60 (1983).
18. Anulewicz R., Krygowski T. M., Pniewska B.: J. Crystallogr. Spectrosc. Res. *17*, 661 (1987).
19. Borisov E. V., Kravtsov D. N., Peregudov A. S., Fedin E. I.: Izv. Akad. Nauk SSSR, Ser. Khim. *1980*, 2151.
20. White N. E., Kilpatrik M.: J. Phys. Chem. *59*, 1044 (1955).
21. Raczynska E. D., Laurence C.: Analyst *116*, 375 (1991).
22. Exner O., Jehlička V.: Collect. Czech. Chem. Commun. *30*, 639 (1965).
23. Exner O., Cook M. J., Howe T. J.: J. Mol. Struct. *240*, 11 (1990).
24. Oszczapowicz J., Orlinski R., Hejchman E.: Pol. J. Chem. *53*, 1259 (1979).
25. Halverstadt I. F., Kumler W. D.: J. Am. Chem. Soc. *64*, 2988 (1942).
26. Vogel A. I.: J. Chem. Soc. *1948*, 1833.
27. Exner O.: *Dipole Moments in Organic Chemistry*, Chap. 3.3. Thieme, Stuttgart 1975.
28. Exner O., Bláha K.: Collect. Czech. Chem. Commun. *42*, 2379 (1977).
29. Oszczapowicz J., Orlinski R.: Pol. J. Chem. *54*, 1901 (1980).
30. Exner O.: Collect. Czech. Chem. Commun. *55*, 1435 (1990).
31. Roberts R. M.: J. Am. Chem. Soc. *72*, 3608 (1950).
32. Šaman D., Exner O.: Unpublished results.
33. Exner O.: *Dipole Moments in Organic Chemistry*, Chap. 3.7. Thieme, Stuttgart 1975.
34. Exner O., Pecka J.: J. Chem. Res., Synop. *1988*, 404.
35. Lumbroso H., Curé J.: J. Mol. Struct. *239*, 219 (1990).
36. Exner O., Waisser K.: Collect. Czech. Chem. Commun. *47*, 828 (1982).

Translated by the author (V. V.).