Stereochemistry and Stereoelectronics of Azines. A Solid State Study of Symmetrical, (*E*,*E*)-Configured, *Para*-Substituted (H, F, Cl, Br, CN) Acetophenone Azines

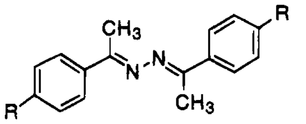
Grace Shiahuy Chen,[1a] Mitchell Anthamatten,
Charles L. Barnes,[1b] and Rainer Glaser*

Department of Chemistry, University of
Missouri—Columbia, Columbia, Missouri 65211

Received April 7, 1994

Introduction

The formation of 1,5-diazabicyclo[3.3.0]octanes via 1,3-dipolar cycloadditions of azines with dienophiles, the *crisscross* addition,[2] plays an important role for the construction of five-membered rings that parallels the significance of the Diels−Alder reaction for six-membered ring systems. The *crisscross* addition is remarkable in that other closely related aza-derivatives react in a Diels−Alder fashion[3] while azines give 1,3-dipolar additions.[4] Aside from the *crisscross* addition, azines react as the "ene" component in [3 + 2] additions,[5] they are becoming increasingly important for C—C bond formations,[6] and they have found many important uses due to their special properties.[7] In light of the great synthetic utility of azines, there has been significant interest in studies of their stereochemistry.[8] We are studying systematically the stereochemistry and the stereoelectronics of azines[9] with focus on 1,4-diphenyl azines. Questions of conjugative interactions are central to these discussions and these questions are usually addressed via analysis of structural data. Deductions regarding electronic structures on the basis of geometries are difficult for two reasons. Intrinsically, the analysis of bonding based on the structural data of a particular azine suffers naturally from the lack of reference data. Furthermore, the magnitude of the structural effects, if any, might be small and difficult to see even if conjugation does occur. To overcome the first problem, examinations of electronic structure require *comparative analysis of a series of closely related molecules and evaluation of the changes of structural parameters*. Here, we report and discuss the crystal structures of five symmetrical acetophenone azines: the parent system 1,4-diphenyl-1,4-dimethyl-2,3-diazabutadiene, **I**, the halogen-disubstituted systems *p*-fluoro- (**II**), *p*-chloro- (**III**), and *p*-bromo- (**IV**) systems, as well as the "pseudo-halogen"-disubstituted *p*-cyano system (**V**). The second problem remains, that is, while our analysis will show that there are no structural indications of conjugative effects, conjugation cannot be completely excluded on the basis of structural data alone.



I , R = H
II , R = F
III , R = Cl
IV , R = Br
V , R = CN

Experimental Section

Azines **I**−**V** were prepared by refluxing acetophenone or the appropriate *para*-substituted derivative with hydrazine hydrate in acidic ethanolic solution.[10] Single crystals were grown from CH$_2$Cl$_2$ solutions via *n*-hexane diffusion. We also prepared pure *p*-iodoacetophenone azine in this fashion but the crystals obtained were not suitable for X-ray analysis. Perspective ORTEPII[11ab] drawings of **I**−**V** with the numbering schemes are depicted in Figure 1 and stereo PLUTO[12] molecular packing diagrams are shown in Figure 2. Experimental details are listed in Table 1 and selected bond lengths, angles, and torsion angles are given in Table 2.

Results and Discussion

The azines **I**−**V** are (*E*,*E*)-configured, consistent with steric demands of the substituents at the azine-C atoms. The parent and the halogen-substituted systems all assume *gauche* conformations with torsion angles τ, C=N—N=C, of 138.7° for **I** and 138.0° (**II**), 134.7° (**III**), and 124.6° (**IV**) for the substituted azines. The halogen-substituted azines show a tendency toward a more distinctly *trans*−*gauche* conformation as the electronegativity[13] of the substituent increases in the order H (2.28) < Br (2.80) < Cl (3.03) < F (3.95). The X-ray structure of the *trans p*-ethyl ester acetophenone azine[14] is in line with the tendency for overall electron-withdrawing *para*-substituents to increase the τ angle, that is, to give more antiperiplanar structures. It thus appears that overall electron-withdrawing substituents tend to increase τ but electronegativity is clearly not the only factor affecting the C=N—N=C conformation. The τ value also is enlarged if the substituent exhibits a π-acceptor ability (e.g. ester, nitrile) and reduced otherwise (halogens). For **II**, these effects nearly cancel and the τ angles of **I** and **II** happen to become nearly identical. The cyano-system **V** realizes a *trans* N—N conformation with τ = 180° and

---

[1] (a) Part of the projected Ph.D. dissertation of G.S.C. (b) Crystallography. (c) Part 2 in a series on "Stereochemistry and Stereoelectronics of Azines", for parts 1 and 3 see refs 9a and 9b.

[2] (a) Grashey, R.; Padwa, A, Azomethine Imines. In *1,3-Dipolar Cycloaddition Chemistry*; Taylort, D. C., Weissberger, A., Eds.; General Heterocyclic Chemistry Series, John Wiley & Sons: New York, 1984; Vol. 1, p 733ff. (b) Wagner-Jauregg, T. *Synthesis* **1976**, 349.

[3] (a) Fringuelli, F.; Taticchi, A. *Dienes in the Diels-Alder Reaction*; John Wiley & Sons: New York, 1990. (b) Ghosez, L. *J. Am. Chem. Soc.* **1975**, *97*, 4409.

[4] Huisgen, R. *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 321.

[5] (a) Prajapati, D.; Sandu, J. S. *Heterocycles* **1985**, *23*, 1123. (b) Schweizer, E. E.; Cao, Z.; Rheingold, A. L.; Bruch, M. *J. Org. Chem.* **1993**, *58*, 4339.

[6] (a) Barluenga, J.; Iglesias, M. J., Gotor, V. J. *Chem. Soc. Chem. Commun.* **1987**, 582; and refs therein. (b) Ikeda, I.; Kogame, Y.; Okahara, M. *J. Org. Chem.* **1985**, *50*, 3640.

[7] (a) Kolb, V. M.; Kuffel, A. C.; Spiwek, H. O.; Janota, T. E. *J. Org. Chem.* **1989**, *54*, 2771. (b) Bell, T. W.; Papoulis, A. T. *Angew. Chem.* **1992**, *104*, 792. *Angew. Chem. Int. Ed. Engl.* **1989**, *31*, 749. (c) Dudis, D. S.; Yeates, A. T.; Kost, D.; Smith, D. A.; Medrano, J. *J. Am. Chem. Soc.* **1993**, *115*, 8770. (d) Espinet, P.; Etxebarria, J.; Marcos, M.; Perez, J.; Remon, A.; Serrano, J. L. *Angew. Chem.* **1989**, *101*, 1076. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1065.

[8] See literature cited in ref 9a. For some recent studies of hetero-substituted azines, see: (a) Hagen, K.; Hedberg, K. *J. Phys. Chem.* **1992**, *96*, 7976. (b) Kober, G.; Rademacher, P.; Boese, R. *J. Chem. Soc. Perkin Trans. 2* **1987**, 761. (c) Kober, G.; Rademacher, P.; Boese, R. *Acta Scand. A* **1988**, *42*, 571.

[9] (a) Glaser, R.; Chen, G. S.; Barnes, C. L. *J. Org. Chem.* **1993**, *58*, 7446. (b) Chen, G. S.; Anthamatten, M.; Barnes, C. L. Glaser, R. *Angew. Chem.*, in press.

[10] Flemming, E.; Harley-Mason, J. *J. Chem. Soc.* **1961**, 5560.

[11] (a) Johnson, C. K. ORTEPII. Report ORNL-5138, Oak Ridge National Laboratory, Tennessee, 1976. (b) Atomic coordinates, structure factors, positional parameters, and anisotropic thermal parameters for I−V were deposited with the Cambridge Crystallographic Data Centre. This material can be obtained from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

[12] Motherwell, W. D. S. *PLUTO. Program for plotting crystal and molecular structures*; University of Cambridge: England, 1976.

[13] Wells, P. R. *Prog. Phys. Org. Chem.* **1968**, *6*, 111.

[14] Ciajolo, M. R.; Sirigu, A.; Tuzi, A. *Acta Cryst.* **1985**, *C41*, 483.

0022-3263/94/1959-4336$04.50/0

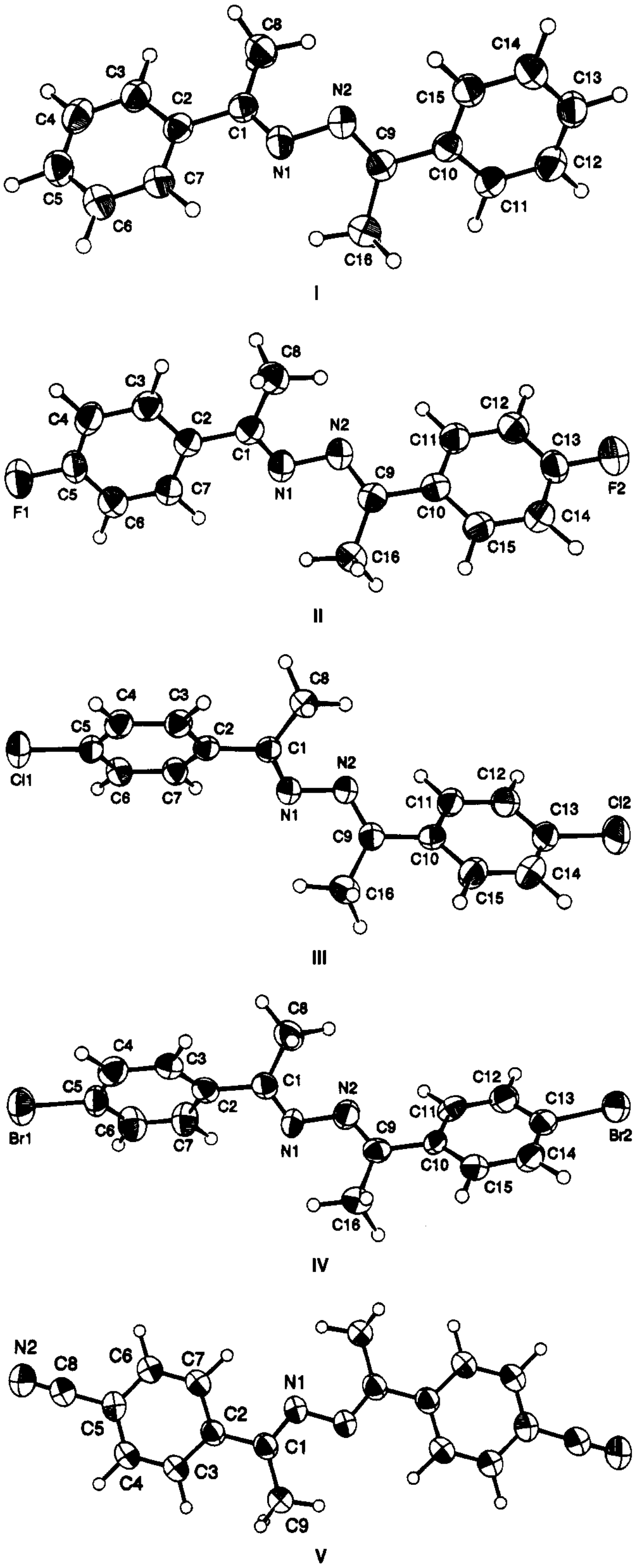


Figure 1. ORTEPII stereodrawings of the azines I−V with the numbering scheme.

overall C_{2h} symmetry. The electronegativity of the CN group is 3.30 and between F and Cl but a *trans* structure results possibly because of the π-acceptor ability of the cyano group.

Small variations in the τ angle require little energy and might therefore be affected by crystal-packing effects.[9a] We analyzed the crystal packing of **I−V** with a view to possible interactions between proximate phenyl groups as well as between phenyl groups and proximate halogen atoms. Importantly, no structural indications of such interactions occur in **I−IV** (see Figure 2) and the shortest intermolecular X⋯X interactions are close to the sum of the van der Waals radii.[15] The crystal of **V** contains layers of stacked azines with alternating stacking directions. Intermolecular stacking interactions between the phenyl groups might in part be responsible for the N−N *trans* conformation of **V** while intermolecular distances between cyano groups are much longer than van der Waals contacts.[15] Hence, the structural differences of **I−IV** would seem to be primarily the result of intrinsic features whereas the structures of **V** and of other related and previously reported azines are affected by specific and strong intermolecular interactions. The solid-state structure of the *p*-hydroxy acetophenone azine[16] shows a τ value of 148°; that is, the HO substituent causes the τ value to become larger than for the parent compound **I** or any of the halogen-substituted systems. The C=N−N=C conformation of this molecule is undoubtedly affected by the strong intermolecular H-bonds formed between the OH groups of one molecule with a crystal water and with the HO group of another neighboring azine. Similarly, the crystal structure of the closely related *p*-(difluoromethoxy)benzylidene azine[17] shows the *trans* conformation ($\tau = 180°$) which is likely to be caused by intermolecular H⋯F hydrogen bonding enhanced by the acidic character of the F_2CH-hydrogen.

The aromatic C−C bonds generally deviate only slightly in the range of 1.380−1.400 Å for **I−V**, but the lengths of the C−C bonds involving the C-atom attached to the substituent differ significantly. The aromatic C−C bonds C4−C5, C5−C6, C12−C13, and C13−C14 lengthen with decreasing X-electronegativity; the average[18] bond lengths for **II−IV** are 1.366 ± 0.003, 1.373 ± 0.008, and 1.380 ± 0.005 Å, respectively, and the bond lengths for **V** are 1.369 and 1.389 Å. The C−C(X)−C angles are 120.31° for **V** and they are less than 121.5° for the halogenated azines **II−IV**. These benzene ring deformations with substituent electronegativity are expected and follow known trends.[19]

Possible electronic interactions of the phenyl substituents with the azine backbone are shown using resonance forms in Scheme 1 (not all are shown). Forms **B** and **C** are degenerate to maintain the overall symmetry of the electron density distribution. Forms **B** and **C** should only be important if the substituents are capable of stabilizing radical density,[20] while **D** should be important if X primarily stabilizes delocalized positive charge. Significant contributions from **B−D** are expected to lengthen the C=N and shorten the C_{ipso}−C bonds, and **B** and **C** would shorten the N−N bond while **D** would lengthen it. Forms **B** and **C** would favor *trans* structures, while

---

(15) Short intermolecular X⋯X interactions (Å). In **II**: F1−F1a 2.950(4), F1−F2b 2.937(3), F2−F1c 2.937. In **III**: Cl1−Cl2a 3.3395(9), Cl2−Cl1b 3.3395(9). In **IV**: Br1−Br2a 3.5604, Br2−Br1b 3.5604(10). In **V**: N2−N2b 3.793. Sum of van der Waals radii (Å): F⋯F 2.94, Cl⋯Cl 3.50, Br⋯Br 3.70, and N⋯N 3.10.

(16) Garcia-Mina, M. C.; Arrese, M.; Martinez-Ripoll, M.; Garcia-Blanco, S.; Serrano, J. L. *Acta Crystallogr.* **1982**, *B38*, 2726.

(17) Sereda, S. V.; Antipin, M. Y.; Timofeeva, T. V.; Struchkov, Y. T. *Sov. Phys. Crystallogr.* **1988**, *33*, 66.

(18) Average values are given with their deviations from the actual bond lengths. The estimated standard deviations for the three bonds (in the same order) are 0.004 (**II**), 0.0035 (**III**), and 0.0085 (**IV**) Å. The esd's for the two C−C bonds in V are 0.003 Å.

(19) Domenicano, A. *Structural Substituent Effects in Benzene Derivatives*, in *Accurate Molecular Structures − Their Determination and Importance*; Domenico, A.; Hargitti, I., Eds.; IUCr/Oxford: University Press, 1992.

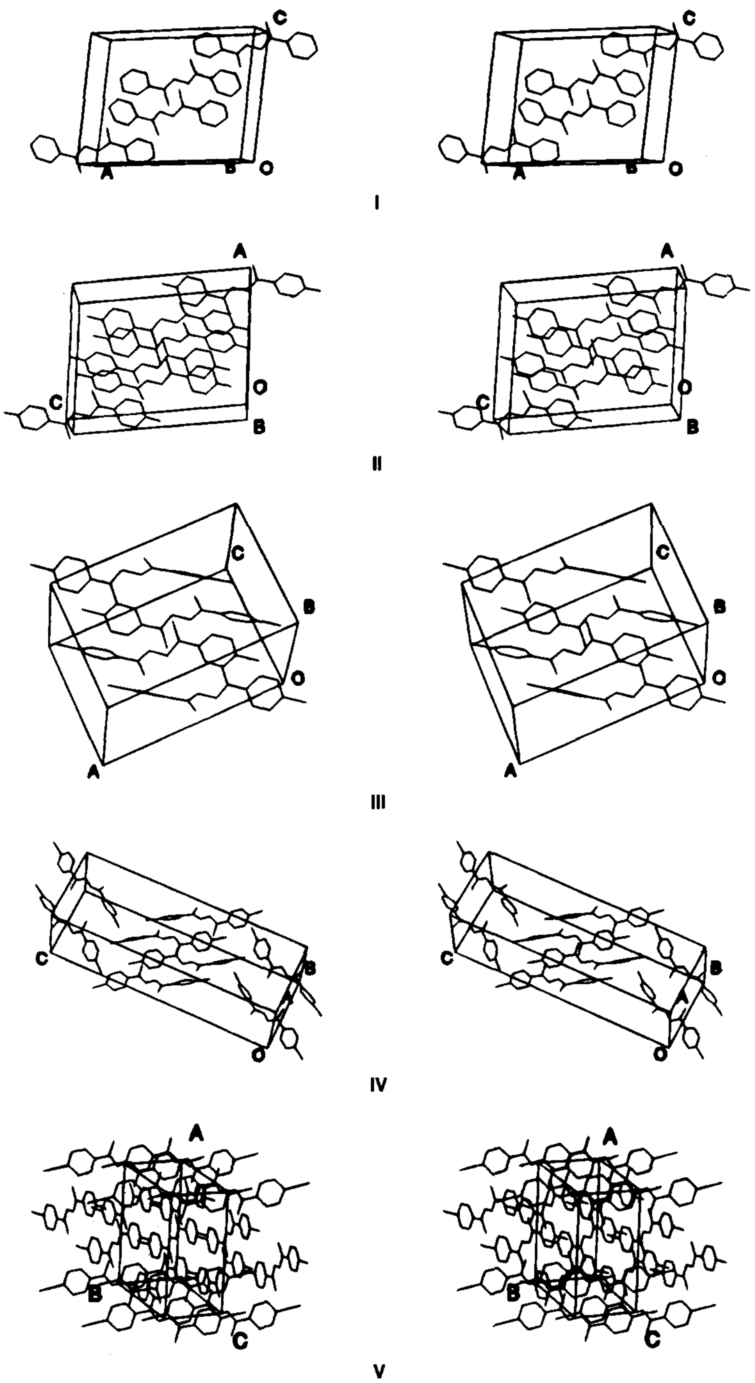


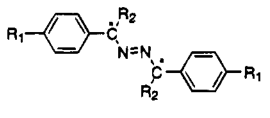
Figure 2. Packing diagrams of **I**–**V**.

the type of conjugation represented by **D**, conjugation within the N-analogue vinylbenzene subsystems of the azine, can be realized in *gauche* structures as well and indeed would be favored in the latter.

The C=N bond lengths of **I**, **II**, **III**, and **V** fall in the range of 1.277–1.288 Å which are close to the 1.279 Å for C_{sp2}=N bond lengths[21] and close to the C=N bond length of 1.276 Å in formaldoxime.[22] Even shorter C=N bond lengths of 1.264 and 1.269 Å occur in **IV**. The N–N bond lengths for **I**–**V** are 1.403, 1.396, 1.398, 1.383, and 1.397 Å, respectively. They are all shorter than 1.47 Å, the generally accepted N–N single bond length[23] and these shortenings are expected for N-N bonds between sp^2-hybridized N-atoms. The C–C bonds between the azine-C and aromatic C-atom are in a range of 1.475–1.490 Å and they are close to 1.485 Å of the normal C_{sp^2}–C_{sp^2} single bond.[24] None of the variations of these bond

---

[20] Note that **B**–**D** all are degenerate. For symmetrical azines the consideration of both **B** forms, for example, includes the consideration of the diradical resonance form shown below. In particular, molecular symmetry therefore *does not* require the contributions of **B**–**D** to be zero.



[21] Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc. Perkin Trans. 2* **1987**, S1.

[22] Levine, I. N. *J. Chem. Phys.* **1963**, *38*, 2326.

[23] Standorfy, C. *General and Theoretical Aspects in the Chemistry of the Carbon-Nitrogen Double Bond*, Patai, S., Ed.; Interscience Publishers: New York, 1970; p 2.

Table 1. Details of Crystallographic Data Collections

	I	II	III	IV	V
crystal color	yellow	yellow	colorless	colorless	yellow
crystal shape (mm)	0.16 × 0.33 × 0.40	0.25 × 0.35 × 0.40	0.20 × 0.35 × 0.35	0.15 × 0.30 × 0.30	0.20 × 0.20 × 0.45
chemical formula	$C_{16}H_{16}N_2$	$C_{16}H_{14}N_2F_2$	$C_{16}H_{14}N_2Cl_2$	$C_{16}H_{14}N_2Br_2$	$C_{18}H_{14}N_4$
formula weight	236.31	272.29	305.20	394.10	286.33
crystal system	monoclinic	monoclinic	monoclinic	orthorhombic	monoclinic
space group	*P*21/*n*	*P*21/*c*	*P*21/*c*	*Pbca*	*P*21/*n*
a	14.8744(8)	11.846(4)	15.0690(20)	9.8150(20)	12.3517(8)
b	7.5556(4)	7.5104(11)	9.344(6)	10.1860(20)	6.9459(5)
c	11.7097(6)	15.379(6)	10.4591(9)	30.601(3)	8.8596
β	97.7520(20)	96.580(20)	94.114(4)		100.987(3)
θ range	$40° \leq 2\theta \leq 50°$	$20° \leq 2\theta \leq 30°$	$20° \leq 2\theta \leq 30°$	$20° \leq 2\theta \leq 30°$	$40° \leq 2\theta \leq 50°$
volume of unit cell (Å^3)	1303.97(12)	1359.2(7)	1469.0(10)	3059.4(9)	746.17(9)
Z	4	4	4	8	2
D_x (g/cm^3)	1.204	1.331	1.380	1.711	1.274
radiation (λ, Å)	Cu Kα (1.54056)	Mo Kα (0.70930)	Mo Kα (0.70930)	Mo Kα (0.70930)	Cu Kα (1.54056)
μ (cm^{-1})	5.2	0.9	4.3	52.4	5.0
maximum value of θ	$2\theta_{max} = 119.7°$	$2\theta_{max} = 46°$	$2\theta_{max} = 46°$	$2\theta_{max} = 46°$	$2\theta_{max} = 129.9°$
h	$-16 \rightarrow 16$	$-13 \rightarrow 12$	$-16 \rightarrow 16$	$0 \rightarrow 10$	$-14 \rightarrow 14$
k	$0 \rightarrow 8$	$0 \rightarrow 8$	$0 \rightarrow 10$	$0 \rightarrow 11$	$0 \rightarrow 8$
l	$0 \rightarrow 13$	$0 \rightarrow 16$	$0 \rightarrow 11$	$0 \rightarrow 33$	$0 \rightarrow 10$
residuals: R; R_w	0.057; 0.086	0.047; 0.062	0.038; 0.066	0.036; 0.043	0.049; 0.079
no. of parameters	164	182	182	181	100
$\Delta\varrho$: max.; min (eÅ^{-3})	0.260; −0.230	0.160; −0.210	0.200; −0.230	0.520; −0.330	0.140; −0.150

Table 2. Selected Bond Lengths (Å), Angles (deg) and Torsion Angles (deg), with esd's in Parentheses

	I	II	III	IV	V
X1—C5		1.356(3)	1.7420(22)	1.904(5)	1.435(5)
X2—C13		1.358(3)	1.7426(24)	1.891(5)	
N1—N2	1.4032(25)	1.396(3)	1.3977(24)	1.383(6)	1.397(3)
N1—C1	1.278(3)	1.284(3)	1.288(3)	1.264(7)	1.277(3)
N2—C9	1.278(3)	1.285(3)	1.282(3)	1.269(7)	
C1—C2	1.490(3)	1.483(3)	1.476(3)	1.478(7)	1.475(3)
C1—C8	1.498(3)	1.498(4)	1.491(3)	1.517(8)	1.497(3)[a]
C9—C10	1.486(3)	1.481(4)	1.475(3)	1.477(7)	
C9—C16	1.500(3)	1.496(4)	1.501(3)	1.503(7)	
N2—N—C1	115.44(18)	116.10(22)	115.26(17)	116.3(5)	113.89(17)
N1—N2—C9	114.52(18)	114.64(21)	115.75(17)	117.0(4)	
N1—C1—C2	115.97(18)	115.75(22)	115.71(18)	118.4(5)	115.21(19)
N1—C1—C8	124.53(19)	123.72(23)	124.45(19)	123.6(5)	125.01(20)[b]
C2—C1—C8	119.49(18)	120.52(23)	119.84(18)	118.0(5)	119.78(18)[c]
C1—C2—C3	121.75(19)	121.42(23)	121.22(19)	122.9(5)	121.66(19)
N2—C9—C10	116.66(19)	116.47(23)	116.33(19)	117.3(5)	
N2—C9—C16	123.83(20)	124.17(23)	124.00(19)	123.7(5)	
C10—C9—C16	119.50(18)	119.36(23)	119.67(19)	119.0(5)	
C9—C10—C11	121.44(19)	120.52(23)	120.45(19)	119.6(5)	
C1—N1—N2—C9	−138.7(2)	138.0(3)	134.7(2)	124.6(6)	180.0
N2—N1—C1—C8	1.6(1)	−3.0(1)	−4.4(1)	−7.3(3)	0.32[d]
N1—N2—C9—C16	3.5(1)	−4.2(1)	−4.5(1)	−4.0(3)	
N2—N1—C1—C2	−179.2(2)	178.2(3)	176.2(2)	172.9(6)	−179.55
N1—N2—C9—C10	−177.9(2)	176.9(3)	176.0(2)	177.5(6)	
N1—C1—C2—C3	−178.2(3)	−178.6(3)	149.7(3)	152.1(7)	−179.9(3)
C8—C1—C2—C3	1.0(1)	2.5(2)	−29.8(1)	−27.6(3)	−0.1(1)
N2—C9—C10—C11	−159.0(3)	−18.6(2)	−30.5(1)	−20.9(3)	
C16—C9—C10—C11	19.8(1)	162.5(3)	149.9(3)	160.5(6)	

[a] C1—C9. [b] N1—C1—C8. [c] C2—C1—C9. [d] N2—N1—C1—C9.

lengths correlate in any significant way with the electronegativity of the substituent or with substituent constants[25] (e.g. σ_p, F, R). Thus, these experimental findings provide *no* convincing evidence for important contributions by forms **B**–**D**. Short C—C and N—N bond lengths of 1.465 and 1.380 Å, respectively, were found in the crystal structure of planar benzal azine[26] and interpreted by Sinha in the sense that the C—C and N—N bonds possessed some double-bond character as a result of conjugation. This conclusion that shorter N—N and C—C bond lengths are indicative of double-bond character resulting from contributions of resonance forms reflecting extensive conjugation over the entire molecule, however, is not a straightforward one because the bond distances do not significantly dependent on the C=N—N=C conformation.[9,27] Moreover, the results presented here show that **I**–**IV** all are *gauche* and that the shortest N—N bond length occurs in the systems with the lowest C=N—N=C torsion angles. Polymorphism of *p*-methylacetophenone azine allowed for the unique opportunity to analyze two conformational C=N—N=C bond isomers, and this analysis provided further compelling evidence against the significance of conjugative interactions in symmetrical

---

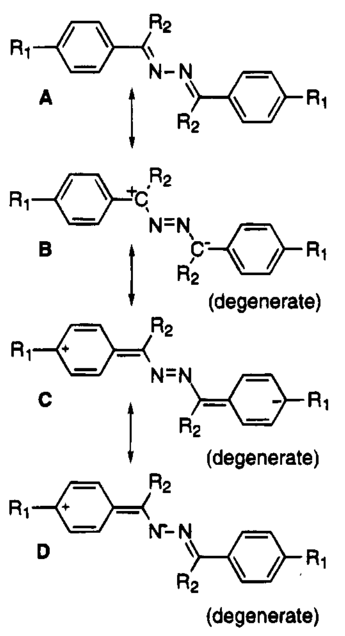
[24] Streitwieser, A., Jr.; Heathcock, C. H. *Introduction to Organic Chemistry*, 3rd ed.; Macmillan Publishing Co.: New York, 1985; p 527.

[25] Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1992**, *91*, 165.

[26] Sinha, U. C. *Acta Crystallogr.* **1970**, *B26*, 889.

[27] Lai, E. C. K.; Mackay, D.; Taylor, N. J.; Watson, K. N. *Can. J. Chem.* **1988**, *66*, 2839. Note that the structure reported in this paper as that of **I** is actually the structure of the azine (PhCH=CHC=N-)$_2$.

Scheme 1



1,4-diphenyl azines and against the importance of the resonance forms suggested by Sinha.[9b]

Another very interesting feature of **I**–**IV** concerns the conformation of the phenyl groups. The N=C—C_{ipso}—C_{ortho} torsion angles, ϕ, not only show that the phenyl groups assume conformations that do not allow for full conjugation with the azine fragment but there also are differences for the conformation of the two phenyl groups *in the same molecule*. For instance, **III** and **IV** have similar ϕ angles of −29.3° and −27.2°, respectively, on one side and −30.5° and −20.9°, respectively, at the other end of the molecule. In the cases of **I** and **II**, however, the differences are more significant: The phenyl rings are twisted only slightly by 0.4° and 1.9°, respectively, on one side but by 19.7° and −18.6°, respectively, on the other. With these structures of **I** and **II** it is therefore possible to examine whether conjugation over the fragment PhC=N occurs, that is, whether **D** is important. Furthermore, one can examine whether this type of conjugation might be more significant than conjugation within the azine moiety. It is found that no matter whether the phenyl rings are twisted or not, the C=N and C_{azine}—C_{ipso} bond lengths on the two sides remain almost the same for **I** and **II**! Although **V** has the planar C_{2h} structure, the C1—C2 and N—N bond lengths are very close to the *gauche* conformation of **III** and the C=N bond lengths are almost the same with **I**.

Our analysis of the solid state structures of a series of acetophenone azines thus shows that there are no convincing structural manifestations either for phenyl conjugation with the entire azine fragment or within the N-analogue vinylbenzene subsystems.

Acknowledgment is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, to the Research Board of the University of Missouri, and to the National Science Foundation for support of this research. MA thanks the Hughes Foundation for an undergraduate research scholarship.