Table I. Rate Constants of Aqueous Iodine Reactions of **1**[a]

run	$10^4[\mathbf{1}]$	pH	[KI]	[KCl]	k_{obsd}, s^{-1}
1	5.17	5.85[b]	0.80	0.20	0.0077
2	5.17	5.85	0.60	0.40	0.0113
3	5.17	5.85	0.40	0.60	0.0150
4	5.17	5.85	0.20	0.80	0.0352
5	5.17	5.85	0.10	0.90	0.0867
6	7.71	9.0[c]	0.80	0.20	11.8
7	7.71	9.0	0.40	0.60	29.5
8	7.71	9.0	0.20	0.80	56.6
9	7.71	9.0	0.10	0.90	149
10	5.17	5.66[b]	0.20	0.80	0.0237
11	3.45	5.66	0.20	0.80	0.0156
12	1.72	5.66	0.20	0.80	0.0090

[a] 26.0 °C, all concentrations in molarity, $[I_3^-]_0 = (3-9) \times 10^{-5}$ M. [b] 0.05 M phosphate. [c] 0.05 M borate.

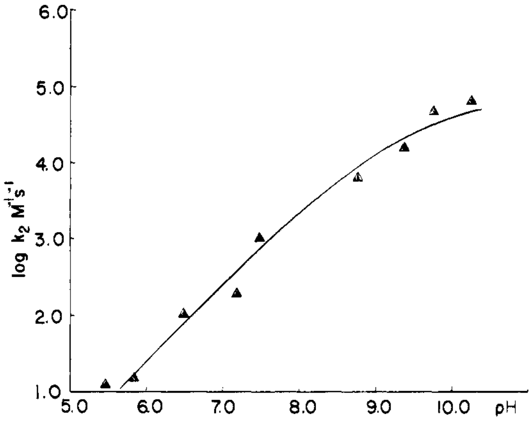


Figure 1. The pH dependence of the I_2 reaction of **1** when [**1**] = (5–8) × 10^{-4} M, [KI] = 0.20 M, [KCl] = 0.80 M, buffer concentrations = 0.0125–0.050 M; the solid curve has been drawn from the equation $k_{obsd} \alpha K_a/(K_a + [H^+])$ where $pK_a = 9.5$.

constants with varying iodide concentrations are listed in runs 1–5 and 6–9. Linear regression of the log k_{obsd} vs. log $[I^-]$ had slopes of −1.15 (pH 5.85) and −1.19 (pH 9.0), both with correlation coefficients of 0.997. Also in Table I (runs 10–12) are the effects of changes in the concentration of **1** on the rate constants. Linear regression of the log k_{obsd} vs. log [**1**] gave a slope of 0.86 and a correlation coefficient of 0.998. Thus, at a given pH, the rate law for the reaction of **1** with I_3^- is $d[I_3^-]/dt = -k'_{obsd}[\mathbf{1}][I_3^-][I^-]^{-1}$. In Figure 1 are plotted the values of log $(k'_{obsd}/[\mathbf{1}])$ vs. pH for the reaction of **1**. The solid line was calculated by using $k_{obsd} \alpha K_a/(K_a + [H^+])$ where $pK_a = 9.5$. These data indicate that an unprotonated amine is the nucleophile in the reaction. The overall rate law is $d[I_3^-]/dt = -k'(K_a/(K_a + [H^+]))[\mathbf{1}][I_3^-][I^-]^{-1}$, and in a given run, $k_{obsd} = k'(K_a/(K_a + [H^+])[\mathbf{1}][I^-]^{-1}$ M s^{-1}. By use of $K_{I_3^-}$ for the equilibrium constant for triiodide formation,

$$d[I_3^-]/dt = -k'(K_a/(K_a + [H^+]))[\mathbf{1}][I_2]K_{I_3^-}$$

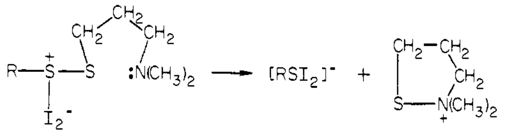
The rate law for **1** is consistent with the mechanism shown in eq 1–3 where R = $(CH_3)_2N(CH_2)_3$–, the unprotonated amine.

$$I_3^- \rightleftharpoons I_2 + I^- \qquad (1)$$

$$I_2 + RSSR \rightleftharpoons RSSR{\cdot}I_2 \qquad (2)$$

$$\underset{\mathbf{3}}{RSSR{\cdot}I_2} \xrightarrow{slow} [RSI_2]^- + \underset{\mathbf{4}}{[RS]^+} \qquad (3)$$

Attack of iodine on unprotonated **1** to give **3** is followed by a rate-determining cleavage of the S–S bond by an intramolecular amine group yielding an N-alkylated sulfenamide **4**. The geometry of the cleavage reaction is suggested by the theoretical model that has been invoked for concomitant electrophilic nucleophilic disulfide cleavage.[10] In this model the electrophile, I_2, attacks in a direction 90° from the S–S bond axis while the nucleophile comes in along an extension of the S–S bond axis.



3

4

Surprisingly, iodine reacts 30 times faster with **1** than with methionine, a reactive acyclic thioether.[11] Compound **1** reacts ~10^6 times faster than its bis quaternary ammonium salt **2**, which is a water-soluble disulfide lacking a neighboring nucleophilic group. The rate constant for the iodine oxidation of **2** is 1 × 10^{-4} s^{-1} when [**2**] = 5.58 × 10^{-4} M and $[I^-]$ = 0.10 M at pH 9.2 *or* 8.2 and increases to 2 × 10^{-4} s^{-1} with a 4-fold decrease in iodide. The insensitivity of the rate constants for **2** to changes in pH or $[I^-]$ also characterized the kinetics of the iodine oxidation of cystine. The slow reaction of **2** with iodine yields the sulfonic acid. The unusual reactivity of **1** has led us to initiate a systematic examination of the effect of other neighboring groups and of other electrophiles on the cleavage of disulfides.

Acknowledgment. We thank the National Science Foundation CHE-80-15489 for support of this research and Dr. J. R. Whitaker, Department of Food Science and Technology, University of California, Davis, for use of the Durrum D-110 stopped-flow spectrophotometer.

---

(9) Because **1** reacts with I_2 at a rate unprecedented for a disulfide it was necessary to ensure that the rapid reaction was not due to thiol impurities, which were not detectable by NMR or GC. By use of conditions of run 4, Table I, where $[I_3^-]$ = 4.7 × 10^{-5} M, the first-order reaction (coefficient of correlation ≥0.999) of I^{3-} goes to completion and has a half-life of 16.5 s. Under the same conditions, but by using solutions 5.27 × 10^{-4} or 5.27 × 10^{-5} M in the thiol, the reaction has a half-life of less than 1 s. When more dilute solutions of thiol were used, a slow, incomplete decay of triiodide was observed and the rate of decay was not first order. Thus, a thiol contaminant could not be responsible for the observed reaction in solutions of **1** under the above conditions.

(10) (a) Rosenfield, R. E.; Parthasarthy, R.; Dunitz, J. D. *J. Am. Chem. Soc.* **1977**, *99*, 4860. (b) Pappas, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 2926.

(11) (a) Gensch, K.-H.; Higuchi, T. *J. Pharm. Sci.* **1967**, *56*, 177. (b) Young, P. R.; Hsieh, L.-S. *J. Am. Chem. Soc.* **1978**, *100*, 7121.

Experimental and Theoretical Studies on Diamagnetic Susceptibility of Amides and Their N-Substituted Derivatives

R. R. Gupta,* M. Kumar, and Rakesh Kumar

Department of Chemistry, University of Rajasthan
Jaipur-302004, India

Received April 21, 1983

Recently, some interesting findings regarding diamagnetic behavior of the C=O group have been reported[1] in aldehydes, ketones, acids, esters, and acyl chlorides. And since, except for some fragmental reports, no systematic studies appear to have been made on the amides, it is therefore, considered interesting to carry out experimental and theoretical studies on amides and their N-substituted derivatives in which C=O group is considerably affected by different existing structural environments.

The magnetic susceptibilities of amides have been measured by the Gouy method.

In order to analyze different existing structural environments and to establish a correlation of χ_M with the structural factors, χ_Ms of these molecules have been calculated theoretically. The Pascal, Pacault, and Hoarau method,[2] based on atomic suscep-

---

(1) (a) Gupta, R. R.; Jain, S. K.; Ojha, K. G. *J. Chem. Phys.* **1977**, *66*, 4961. (b) Mital, R. L.; Gupta, R. R. *Ibid.* **1971**, *54*, 3230.

(2) Pascal, P.; Pacault, A.; Hoarau, J. Compt. R. *Hebd. Seances, Acad. Sci.* **1951**, *233*, 1078.

tibility concept, has been applied by using susceptibility contributions of different atoms present in the molecules and the correction term for a methyl group. The Pascal, Gallais, and Labarre method,[3] which is based on the bond susceptibility concept and considers χ_M to be contributed by susceptibility contributions of bonds, has been used to calculate χ_M by considering bond susceptibility data for diffeent bonds present in the amides and their N-substituted derivatives. A wave–mechanical approach[4] has also been applied to evaluate theoretical χ_M by using the contributions of (i) inner-shell electrons of each atom present, (ii) bonding electrons in each bond, (iii) nonbonding lone pair electrons present in the outer shell, and (iv) π-electrons in the form of expression 1. The theoretical results of χ_M are summarized in Table II.

$$\chi_M = \sum\chi_{\mathrm{ISE}} + \sum\chi_{\mathrm{BE}} + \sum\chi_{\mathrm{NBE}} + \sum\chi_{\pi\text{-electrons}} \qquad (1)$$

A critical perusal of the theoretical and experimental results of χ_M reveals that neither the Pascal, Pacault, and Hoarau method nor the Pascal, Gallais, and Labarre method provides satisfactory results for most of the compounds. The former method gives acceptable results for the amides, but fails to give satisfactory results for most of the N-substituted amides. In this method although a correction term is applied for a methyl group, and therefore different values are obtained for normal and iso isomers, the contributions for structral characteristics have not been accounted for. χ_Ms calculated by the Pascal, Gallais, and Labaree method deviate considerably from their corresponding experimental values for most of the compounds. And such discrepancies between experimental and theoretical χ_M may be attributed to the bond–bond interactions, which have not been duly accounted for in determining bond susceptibility data. Theoretical χ_Ms evaluated by the wave–mechanical approach deviate considerably from their corresponding experimental value, and the same values have been obtained for normal and iso isomers. Therefore, it can be obviously stated that the wave–mechanical calculations also are not suitable at all for the series of investigated amides. Although in the wave–mechanical approach contributions of all types of electrons have been taken into account, still the agreement between experimental and theoretical values is not satisfactory. The reasons for this poor agreement are the structural factors and the interactions between different atoms and groups, which do contribute considerably to the molecular diagmagnetism and have not been accounted for in calculating bond susceptibility data wave–mechanically. The Haberditzl method,[5] in which χ_M is considered to be contributed by (i) inner-shell core electrons, (ii) bonding electron increments, and (iii) π-electrons, although gives due considerations to the contributions of all types of structural factors, could not be applied to the amides and their N-substituted derivatives due to nonavailability of bond susceptibility data for the $(C_3{}^+{=}O^+){-}N_1$ bond.

Since none of the above considered methods has provided satisfactory results of theoretical χ_M, the semiempirical approach,[6-8] in which χ_M is considered to be contributed by (i) atoms, (ii) bonds, and (iii) bond–bond interactions in the form of expression 2, has been developed and applied for amides and their

$$\chi_M = \sum\chi_{\mathrm{atoms}} + \sum\chi_{\mathrm{bonds}} + \sum\chi_{\text{bond–bond interactions}} \qquad (2)$$

N-substituted derivatives and provided excellent results.

In the semiempirical approach, χ_M of amides and their N-substituted derivatives have been paramatized by using different parameters in a specific combination for the different structural environments persisting in the investigated molecules. χ_M for the amides and their N-substituted derivatives (RC(=O) - NR_1R_2) can be expressed by the following combination of parameters:

$$\chi_M = \chi_R + \chi_C + \chi_O + \chi_N + \chi_{R_1} + \chi_{R_2} + \chi_{RC} + \chi_{CO} + \chi_{CN} + \chi_{NR_1} + \chi_{NR_2} - \chi_{RC:CO} - \chi_{RC:CN} - \chi_{CO:CN} - \chi_{CN:NR_1} - \chi_{CN:NR_2} - \chi_{NR_1:NR_2} \qquad (3)$$

Table I. Values of Parameters

parameters	values[a]
A	17.08
B	11.68
C	0.83
D	16.67
E	11.57
F	11.48
G	11.63
H	−0.87
I	11.63

[a] -1×10^{-6} μg/(G^2 mol).

The parameters used in the semiempirical expression represent contributions of atoms, bonds, and bond–bond interactions and can be reduced into the following parameters:

$$A = \chi_C + 4\chi_{CH} + \chi_{CC:CC} - 2\chi_{CC:CH} - 5\chi_{CH:CH}$$

$$B = \chi_C + \chi_{CC} + 2\chi_{CH} - \chi_{CC:CC} - 4\chi_{CC:CH} - \chi_{CH:CH}$$

$$C = 2\chi_{CC:CH} - \chi_{CC:CC} - \chi_{CH:CH}$$

$$D = \chi_C + \chi_O + \chi_N + \chi_{CO} + \chi_{CC} - \chi_{CH} + 2\chi_{NH} + \chi_{CN} + \chi_{CC:CH} - \chi_{CO:CC} - \chi_{CO:CN} - 2\chi_{CN:NH} - \chi_{NH:NH} - \chi_{CN:CC}$$

$$E = \chi_C + \chi_{CC} + 2\chi_{CH} - \chi_{CC:CC} - 4\chi_{CC:CH} - \chi_{CH:CH}$$

$$F = \chi_C + \chi_O + \chi_N + \chi_{CO} + 2\chi_{CN} + \chi_{NH} + 3\chi_{CC:CH} - \chi_{CO:CC} - \chi_{CO:CN} - 2\chi_{CN:NH} - 3\chi_{CN:CN}$$

$$G = \chi_C + \chi_{CC} + 2\chi_{CH} - \chi_{CC:CC} - 4\chi_{CC:CH} - \chi_{CH:CH}$$

$$H = \chi_{CC:CH} + \chi_{CN:CH} + 2\chi_{CN:CN} - \chi_{CH:CH}$$

$$I = \chi_C + \chi_{CC} + 2\chi_{CH} - \chi_{CC:CC} - 4\chi_{CC:CH} - \chi_{CH:CH}$$

The parameter A represents end effects. The parameters B, E, G, and I account for the susceptibility contributions of methylene groups and parameters D and F correspond to the contributions of functional groups in amides and their N-substituted derivatives. Additional parameters C and H stand for the isomeric effects and interactions, respectively. The values of all the parameters have been calculated by using least-squares deviation and are summarized in Table I. Semiempirical χ_{M_s} have been calculated by these parameters and are summarized along with parametric representations in Table II.

χ_M calculated semiempirically agree excellently with the corresponding experimental values for the entire series of amides, since the semiempirical approach, in fact, accounts for almost all the structural factors persisting in these molecules and contributing considerably to the molecular diamagnetism.

The diamagnetic susceptibility contributions of CH_2, C=O, and/an oxygen atom have been evaluated in amides and their N-substituted derivatives and are summarized in Table III. The contribution of the CH_2 group is nearly the same and is not considerably affected by the different existing structural environments. The susceptibility contribution of the C=O group is different in these series, as it is not much changed when amide is converted into an *N*-alkyl derivative while the difference is significant when an *N*-alkyl derivative is changed to an *N*,*N*-dialkyl derivative.

The susceptibility contribution of the oxygen atom is 0.24 units in unsubstituted amides while in *N*-alkyl derivatives is -0.39 units,

---

[3] Pascal, P.; Gallais, F.; Labarre, J. F. Compt. R. *Hebd. Seances Acad. Sci.* **1951**, *252*, 2644.

[4] Baudet, J.; Tillieu, J.; Guy, J. Compt. R. *Hebd. Seances Acad. Sci.* **1957**, *244*, 2920. (b) Baudet, J. *J. Chim. Phys.* **1961**, *58*, 328.

[5] Haberditzl, W. *Saber dt. Akad. Wiss.* (*Kl. Chem. Geol. Biol.*) **1964**, *2*, 34.

[6] Hameka, H. F.; O'Sullivan, P. S. *J. Chem. Phys.* **1961**, *34*, 1996; *J. Am. Chem. Soc.* **1970**, *92*, 25; 1821.

[7] Flygare, W. H.; Burnham, A. K.; Lee, J.; Schmalz, T. G.; Beak, P. *J. Am. Chem. Soc.* **1977**, *99*, 1836.

[8] Mital, R. L.; Gupta, R. R. *J. Am. Chem. Soc.* **1969**, *90*, 4664. Gupta, R. R.; Kumar, M.; Ojha, K. G. *J. Chem. Phys.* **1981**, *75*, 4173; **1982**, *76*, 1173, 5182; **1983**, *79*, 3410.

Table II. Diamagnetic Susceptibilities of Amides

				$\chi_M{}^c$			
				(theoretical)			
compound	parameters	$\chi_M{}^c$ (exptl)	$\chi_M{}^c$ (others)	Pascal, Pacault, and Hoarau method	Pascal, Gallais, and Labarre method	wave-mechanical method	semiempirical method
1. acetamide	$A + D$	33.87	34.08[a] 34.1[b]	33.61	35.17	36.88	33.75
2. propionamide	$A + B + D$	45.47	45.52[a]	44.97	46.57	48.23	45.43
3. butyramide	$A + 2B + D$	57.10	57.16[a]	56.33	57.97	59.58	57.11
4. isobutyramide	$A + 2B + C + D$	57.93	57.99[a]	57.18	58.17	59.58	57.94
5. valeramide	$A + 3B + D$	68.75	69.04[a]	67.69	69.37	70.93	68.79
6. isovaleramide	$A + 3B + C + D$	69.62	69.89[a]	68.54	70.57	70.93	69.62
7. hexamide	$A + 4B + D$	80.47	80.62[a]	79.05	80.77	82.28	80.47
8. *N*-methylacetamide	$A + E + F$	45.22		45.82	47.74	48.70	45.13
9. *N*-ethylacetamide	$A + 2E + F$	56.83		57.18	59.14	60.05	56.70
10. *N*-propylacetamide	$A + 3E + F$	68.09	65.19[b]	68.54	70.50	71.40	68.27
11. *N*-isopropylacetamide	$A + C + 3E + F$	68.82	68.71[b]	69.39	71.70	71.40	69.10
12. *N*-butylacetamide	$A + 4E + F$	79.69	80.21[b]	79.90	81.90	82.75	79.84
13. *N*-isobutylacetamide	$A + C + 4E + F$	80.25	78.87[b]	80.75	83.10	82.75	80.67
14. *N,N*-dimethylacetamide	$A + 2G + 2F - D + H$	55.82	56.08[b]	58.03	58.51	60.52	55.76
15. *N,N*-diethylacetamide	$A + 6G + 2F - D + H$	79.03	77.45[b]	80.75	81.31	82.22	79.02
16. *N,N*-dipropylacetamide	$A + 6G + 2F - D + H$	102.34		103.47	104.11	105.92	102.28
17. *N,N*-dimethylpropionamide	$A + 3I + 2F - D + H$	67.28		69.39	69.91	71.87	67.39
18. *N,N*-diethylpropionamide	$A + 5I + 2F - D + H$	90.62		92.11	92.71	94.57	90.65
19. *N,N*-dipropylpropionamide	$A + 7I + 2F - D + H$	113.81		114.83	115.50	117.27	113.91

[a] Goyal, R. D. Ph.D. Thesis, University of Rajasthan, Jaipur, India, 1972. [b] Angus, W. R. "Diamagnetic Susceptibilities"; Springer-Verlag: West Berlin, 1967; Landoldt-Bornstein Series. [c] -1×10^{-6} μg/(G² mol).

Table III. Magnetic Contributions of the Methylene Group, C=O Group, and Oxygen Atom in Amides

series	equation of linear relationship between χ_M and n	$\chi_{CH_2}{}^a$	$\chi_{CO}{}^a$	$\chi_O{}^a$ (oxygen attached to carbon by double bond)
$H(CH_2)_nC(=O)NH_2$	$\chi_M = 11.68n + 22.64$	11.68	7.64	0.24
$CH_3C(=O)NH(CH_2)_nH$	$\chi_M = 11.57n + 33.74$	11.57	7.11	−0.39
$CH_3C(=O)N[(CH_2)_nH]_2$	$\chi_M = 11.63n + 32.54$	11.63	5.91	−1.49
$C_2H_5C(=O)N[(CH_2)_nH]_2$	$\chi_M = 11.63n + 44.05$	11.63	5.71	−1.71

[a] -1×10^{-6} μg/(G² mol).

which shows the different nature of the oxygen atom: diamagnetic in unsubstituted amides and paramagnetic in *N*-alkyl derivatives. Oxygen has also paramagnetic behavior in *N,N*-dialkyl derivatives but differs considerably in magnitude from that of *N*-alkyl derivatives.

Hence, these observations suggest that the diamagnetic susceptibility contributions of a C=O group and an oxygen atom depend on the electronic environments in which they are present.

Registry No. Acetamide, 60-35-5; propionamide, 79-05-0; butyramide, 541-35-5; isobutyramide, 563-83-7; valeramide, 626-97-1; isovaleramide, 541-46-8; hexamide, 628-02-4; *N*-methylacetamide, 79-16-3; *N*-ethylacetamide, 625-50-3; *N*-propylacetamide, 5331-48-6; *N*-isopropylacetamide, 1118-69-0; *N*-butylacetamide, 1119-49-9; *N*-isobutylacetamide, 1540-94-9; *N,N*-dimethylacetamide, 127-19-5; *N,N*-diethylacetamide, 685-91-6; *N,N*-dipropylacetamide, 1116-24-1; *N,N*-dimethylpropionamide, 758-96-3; *N,N*-diethylpropionamide, 1114-51-8; *N,N*-dipropylpropionamide, 1114-59-6.