CONFORMATIONAL ANALYSIS OF SUBSTITUTED PHENYLACETALDEHYDES BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

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DONALD WILLIAM BUSHMAN
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This is to certify that the

thesis entitled

Conformational Analysis of Substituted Phenylacetaldehydes by Nuclear Magnetic Resonance Spectroscopy

presented by

Donald William Bushman

has been accepted towards fulfillment
of the requirements for

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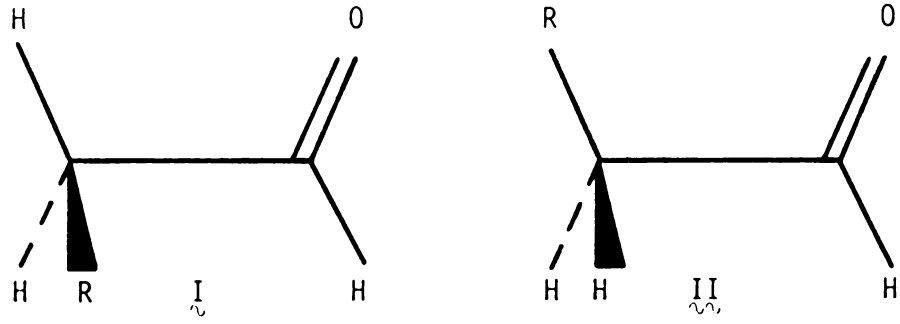
ABSTRACT

CONFORMATIONAL ANALYSIS OF SUBSTITUTED PHENYLACETALDEHYDES BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

By

Donald William Bushman

Nuclear magnetic resonance spectroscopy has been used in the conformational analysis of substituted phenylacetaldehydes. The time averaged vicinal spin-spin coupling constants between the aldehydic and α-protons of phenylacetaldehyde, p-methylphenylacetaldehyde, p-methoxyphenylacetalhyde, p-chlorophenylacetaldehyde, 2,6-dichlorophenylacetaldehyde, and phenylmercaptoacetaldehyde were studied at 60 MHz as a function of temperature and solvent. The data for the substituted phenylacetaldehydes were interpreted in terms of conformations I and II, in which a single bond eclipses the carbonyl group. The analysis of the data led to the following conclusions for the substituted phenylacetaldehydes. 1) Conform-



I II

ation II has a lower enthalpy than I in solvents of high dielectric constant, 2) as the dielectric constant of the solvent is increased the stability of II relative to I increases, 3) the free energy differences for

I ⇄ II are solvent dependent, being more negative in solvents of high dielectric constant, and 4) local dipole-dipole interactions are more important in determining rotamer stability than overall dipole-dipole interactions.

The following conclusions were drawn for phenylmercaptoacetaldehyde. 1) Conformation I is favored by enthalpy relative to II in all solvents studied, 2) as the dielectric constant of the solvent is increased the stability of I relative to II decreases, 3) the free energy differences for I ⇄ II are solvent dependent, being more positive in solvents of low dielectric constant, and 4) the local dipole-dipole interactions are more important in determining rotamer stability than overall dipole-dipole interactions.

Chemical shifts of the aldehydic and methylenic protons were also measured in conjunction with the coupling constants. It was found that the chemical shift results are in agreement with a recent model for the anisotropy of the carbonyl group. These data also reinforce the conclusion derived from the coupling constant data concerning the stability of the rotamers, I and II.

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By

Donald William Bushman

A THESIS

Submitted to
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DOCTOR OF PHILOSOPHY

Department of Chemistry

1971

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AND

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Die Gedanken sind frei!

Wer kann sie erraten?

Sie fliehen vorbei

wie nächtliche Schatten.

Kein Mensch kann sie wissen,

kein Jäger erschiessen,

es bleibet dabei:

Die Gedanken sind frei!

Volksweise aus der
Schweiz um 1815

TABLE OF CONTENTS

Page

INTRODUCTION 1

RESULTS 5

A. Spin-Spin Coupling Constants 5
B. Chemical Shifts 19

DISCUSSION 29

A. Spin-Spin Coupling Constants 31
B. The Effect of Solvent Polarity on Rotamer Stabilities . . .41
C. Chemical Shifts 47

EXPERIMENTAL 49

A. Reagents and Compounds 49
B. Solvents 49
C. Synthesis 49
I. p-Methylphenylacetaldehyde 49
II. p-Methoxyphenylacetaldehyde 50
III. p-Chlorophenylacetaldehyde 51
IV. 2,6-Dichlorophenylacetaldehyde 51
V. Phenylmercaptoacetaldehyde 52
D. N.M.R. Spectra 53

REFERENCES 54

LIST OF TABLES

Table		Page
I.	Vicinal Spin-Spin Coupling Constants, in Hz, of Substituted Phenylacetaldehydes and Phenylmercaptoacetaldehyde.	6
II.	Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of Phenylacetaldehyde	7
III.	Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of p-Methylphenylacetaldehyde	8
IV.	Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of p-Methoxyphenylacetaldehyde	9
V.	Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of p-Chlorophenylacetaldehyde	10
VI.	Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of 2,6-Dichlorophenylacetaldehyde	11
VII.	Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of Phenylmercaptoacetaldehyde	12
VIII.	Solvent Dependence of the Chemical Shifts of Substituted Phenylacetaldehydes and Phenylmercaptoacetaldehyde	20
IX.	Temperature Dependence of the Chemical Shifts of Phenylacetaldehyde	22
X.	Temperature Dependence of the Chemical Shifts of p-Methylphenylacetaldehyde	23
XI.	Temperature Dependence of the Chemical Shifts of p-Methoxyphenylacetaldehyde	24
XII.	Temperature Dependence of the Chemical Shifts of p-Chlorophenylacetaldehyde	25
XIII.	Temperature Dependence of the Chemical Shifts of 2,6-Dichlorophenylacetaldehyde	27
XIV.	Temperature Dependence of the Chemical Shifts of Phenylmercaptoacetaldehyde	29
XV.	Solvent Dependence of the Relative Rotamer Populations of Substituted Phenylacetaldehydes	34

XVI. Solvent Dependence of the Free Energy Differences, $\Delta G°$, Between Rotamers of Substituted Phenylacetaldehydes 35

XVII. Solvent Dependence of the Enthalpy Differences, $\Delta H°$, Between Rotamers of Substituted Phenylacetaldehydes 37

XVIII. Solvent Dependence of the Relative Rotamer Populations of Phenylmercaptoacetaldehyde 38

XIX. Solvent Dependence of the Free Energy Difference, $\Delta G°$, and the Enthalpy Difference, $\Delta H°$, Between Rotamers of Phenylmercaptoacetaldehyde 39

LIST OF FIGURES

Figure | Page

1. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for Phenylacetaldehyde 13

2. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for p-Methylphenylacetaldehyde 14

3. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for p-Methoxyphenylacetaldehyde 15

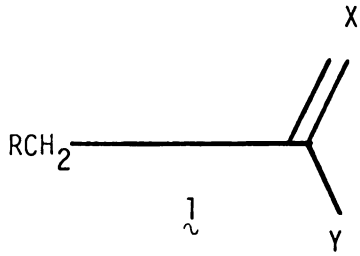
4. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for p-Chlorophenylacetaldehyde 16

5. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for 2,6-Dichlorophenylacetaldehyde 17

6. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for Phenylmercaptoacetaldehyde 18

INTRODUCTION

Many techniques have been used in the investigation of rotational isomerism about carbon-carbon single bonds. Particular attention has been paid to the relative stabilities of rotamers in systems such as 1. The relative stabilities of rotamers 2a and 2b, and 3 have been studied with respect to rotation about the carbon-carbon bond joining the



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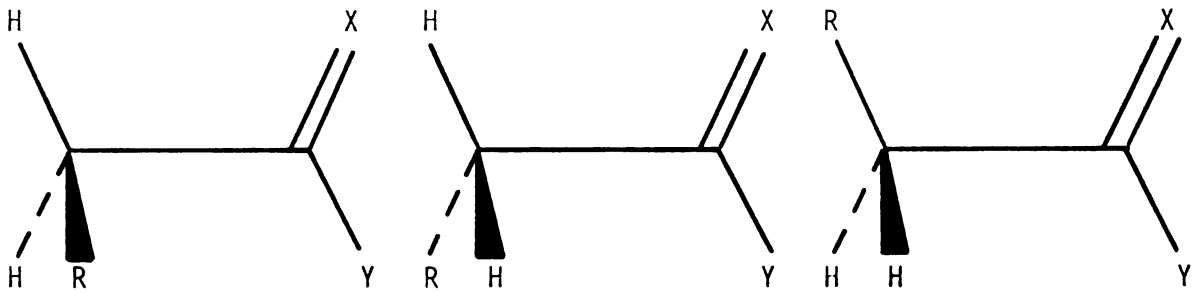
sp^2 and sp^3 hybridized carbons as a function of X, Y, and R. These investigations include Raman and infrared studies of α-haloacetones



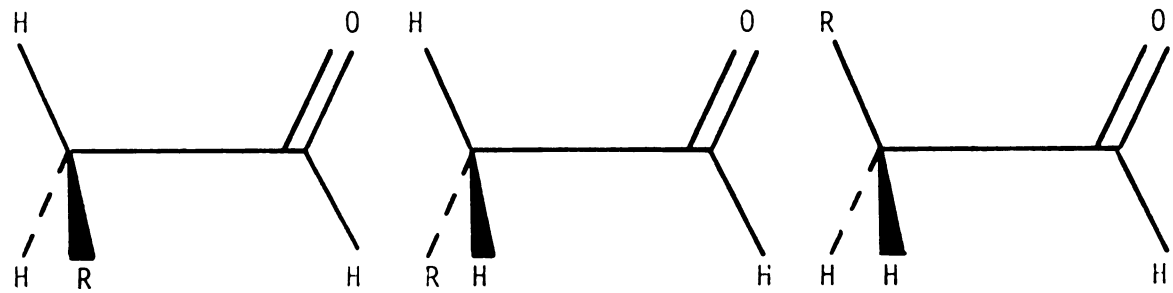
(1,2,3), haloacetylhalides (4,5), and α-haloacetaldehydes (6); microwave studies of acetaldehyde (7), acetone (8), propionaldehyde (9), fluoroacetyl fluoride (10), and olefins (11,12); electron defraction studies of aliphatic ketones (13) and aldehydes (14,15,16); and

nuclear magnetic resonance studies of ketones (17), 3-substituted propylenes (18-22), hydrazones (23,24,25), and aldehydes (26-31).

Several basic factors have been proposed to explain the results of many of these investigations. Included among these factors are nonbonded (attractive and repulsive), dipole-dipole, dipole-induced dipole, and electrostatic interactions. Thus, nonbonded repulsions between R and Y as well as electrostatic dipole-dipole interactions in rotamers 2a and 2b have been used to explain the different 2(a and b)/3 ratios in chloroacetone (1) and chloroacetyl chloride (4). In agreement with this hypothesis are reports using I.R. techniques (6,28), that chloroacetaldehyde exists essentially in conformation 2, conformer 2 being about 300-1500 cal/mole more stable than 3 according to $\Delta H°$ values. However, N.M.R. results (28) have shown 3 to be more stable than 2. It has been shown (29) that in nonpolar solvents 2 for dichloroacetaldehyde is about 300 cal/mole more stable than 3 according to $\Delta H°$ values. In polar solvents, however, dipole-dipole interactions become sufficiently important in dichloroacetaldehyde to make 3 more stable than 2 by 450-1400 cal/mole according to $\Delta H°$ values. Since both conformers 2 and 3 are present in chloroacetone, it might be concluded that nonbonded interactions between R and Y significantly affect the relative stabilities of 2 and 3. In contrast, nonbonded interactions play minor roles on the stabilities of rotamers of aldehydic systems (X = O, Y = H, and R = alkyl or aryl) (27). For example, $\Delta H°$ for $2 \rightleftharpoons 3$ is -800 and -500 cal/mole when R is methyl or isopropyl, respectively. When R is methyl, less than 200 cal/mole of the 800 cal/mole is due to nonbonded repulsions. Nonbonded repulsions only become significant when R is t-butyl, in which case 2 is favored over 3 by 250 cal/mole.

Although for discussion purposes the threefold barrier to rotation is considered and spoken of as having perfectly eclipsed minimum energy conformations, we recognize that N.M.R. techniques cannot detect small deviations in the dihedral angle (27,32).

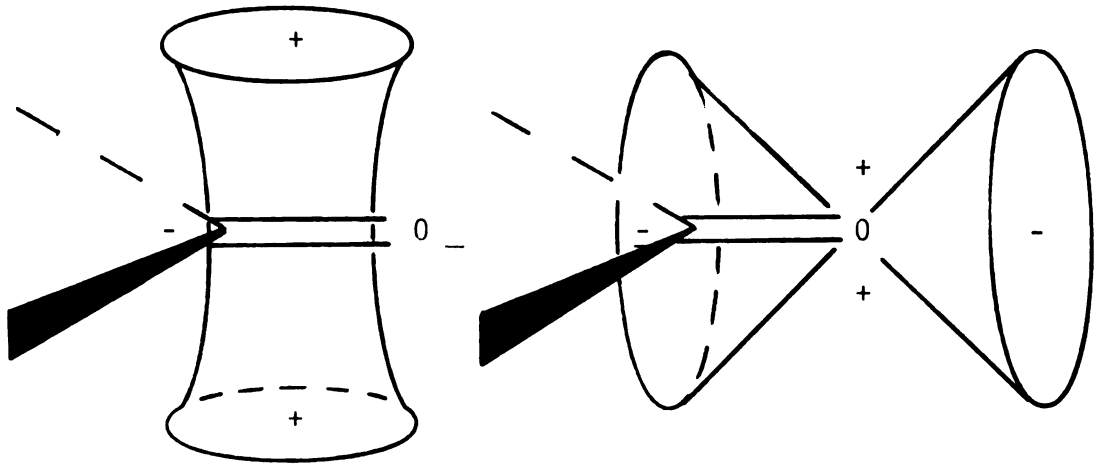
Previous work (30) has indicated that dipole-induced dipole interactions do not play major roles in determining the relative stabilities of 4a, 4b, and 5. However, since dipole-dipole interactions may be significant and since logical substrate choices such as chloro- and bromoacetaldehydes suffer from nonbonded interactions, it is interesting to study the rotational isomerism in substituted phenylacetaldehydes to see the effect of such substitution on the relative



stabilities of 4 and 5. Two possibilities immediately come to mind: 1) that the dipole of the entire group, R, (i.e., phenyl and substituent) will affect the relative stabilities of 4 and 5 or 2) that only local dipole-dipole interactions are important and therefore, substitution should not greatly affect the relative stabilities of 4 and 5.

The effect of the anisotropy of the carbonyl group has been the subject of investigations in recent years (33,34). A model, 6, described by Jackman (35) has been widely accepted; however, a more

refined model, $\underset{\sim}{7}$, has recently been suggested (36). In order to



$\underset{\sim}{6}$ $\underset{\sim}{7}$

determine the agreement of the newer model, $\underset{\sim}{7}$, with experimental results, the chemical shifts of the substituted phenylacetaldehydes and phenylmercaptoacetaldehyde were also measured.

RESULTS

A. Spin-Spin Coupling Constants

The vicinal spin-spin coupling constants for the substituted phenylacetaldehydes and phenylmercaptoacetaldehyde are summarized in Table I. The coupling constants were measured in 5% (vol./vol. for liquids or wt./wt. for solids) solutions in the various solvents and are an average of six to ten measurements with a precision of $\pm$0.03 Hz. They were checked for accuracy against the known values (26,37) of acetaldehyde; 2.85, 2.88, and 2.90 Hz at 36, 0, and -30°, respectively.

The coupling constants of the phenylacetaldehydes proved to be smaller than those of acetaldehyde, as are those of monosubstituted alkyl acetaldehydes (27). These decreased with increasing dielectric constant of the solvent, except in the case of 2,6-dichlorophenylacetaldehyde which behaved erratically. In contrast, the coupling constants for phenylmercaptoacetaldehyde were larger than those of acetaldehyde and again decreased with increasing solvent dielectric constant.

The temperature dependence of the coupling constants are given in Tables II, III, IV, V, VI, and VII. Plots of the coupling constants versus temperature are given in Figs. 1, 2, 3, 4, 5, and 6. The coupling constant of phenylacetaldehyde decreased with increasing temperature in cyclohexane and decalin, was constant in ethyl ether, and increased in methylene bromide, dimethyl formamide, and benzonitrile. As may be seen in Fig. 1, the coupling constant for phenylacetaldehyde becomes independent of temperature at a value of 2.40 Hz. The same

Table I. Vicinal Spin-Spin Coupling Constants[a], in Hz, of Substituted Phenylacetaldehydes and Phenylmercapto-acetaldehyde

Solvent[b]	$PhCH_2CHO$	p-CH_3PhCH_2CHO	p-CH_3OPhCH_2CHO	p-$ClPhCH_2CHO$	2,6-Cl_2PhCH_2CHO	$PhSCH_2CHO$
cyclohexane	2.46	2.52		2.20	1.19	3.28
trans-decalin	2.48	2.50		2.18	1.22	3.27
CCl_4		2.51			1.18	
$(CH_3CH_2)_2O$	2.43	2.50	2.50	2.13	1.14	3.15
THF	2.33		2.41	2.00	1.04	3.00
$CHCl_3$		2.45			1.19	
CH_2Br_2	2.28	2.30	2.27	2.02	1.15	3.17
CH_2Cl_2		2.27			1.10	
$(CH_3)_2CO$					0.90	
$(CH_3)_2NCHO$	2.09	2.15	2.16	1.79	0.76	2.77
C_6H_5CN	2.14	2.17	2.20	1.83	0.97	2.93

[a]Values at 38 ± 2°. [b]5% solutions.

Table II. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of Phenylacetaldehyde

Solvent[a]	J_{HH}, Hz							
	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane				2.44	2.46	2.43	2.38[b]	
trans-decalin	2.45	2.46	2.47	2.46	2.48	2.44	2.44	2.39
$(CH_3CH_2)_2O$	2.43	2.44	2.42	2.45	2.43			
THF					2.33			
CH_2Br_2	2.09	2.13	2.17	2.21	2.28	2.28	2.28	
$(CH_3)_2NCHO$	1.84	1.85	1.96	1.99	2.09	2.09	2.12	2.14
C_6H_5CN			2.02	2.08	2.14	2.16	2.17	2.20

[a] 5% solutions. [b] Value at 80°.

Table III. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of p-Methylphenylacetaldehyde

Solvent[a]	J_{HH}, Hz							
	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane				2.56	2.52	2.51	2.47[b]	
trans-decalin	2.54	2.56	2.56	2.54	2.50	2.48	2.44	2.44
$(CH_3CH_2)_2O$		2.51	2.48	2.49	2.50			
CH_2Br_2	2.00	2.17	2.18	2.26	2.30	2.30	2.24	
$(CH_3)_2NCHO$	1.85	2.01	2.06	2.08	2.15	2.16	2.17	2.20
C_6H_5CN			2.13	2.13	2.17	2.19	2.25	2.24

[a] 5% solutions. [b] Value at 80°.

Table IV. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of p-Methoxyphenylacetaldehyde

Solvent[a]	J_{HH}, Hz							
	-30°	-15°	0°	15°	38°	60°	90°	120°
$(CH_3CH_2)_2O$	2.53	2.50	2.53	2.53	2.50			
THF	2.35	2.40	2.39	2.37	2.41	2.40		
CH_2Br_2	2.14	2.22	2.21	2.28	2.27	2.32	2.37	
$(CH_3)_2NCHO$	2.05	2.04	2.10	2.12	2.16	2.18	2.23	2.24
C_6H_5CN			2.15	2.15	2.20	2.25	2.25	2.29

[a] 5% solutions.

Table V. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of p-Chlorophenylacetaldehyde

Solvent[a]	J_{HH}, Hz							
	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane				2.13	2.20	2.19	2.17[b]	
trans-decalin			2.13	2.13	2.18	2.20	2.21	2.20
$(CH_3CH_2)_2O$			1.92	2.05	2.13			
THF		1.85	1.88	2.00	2.00	2.05		
CH_2Br_2	1.82	1.80	1.79	1.98	2.02	2.06	2.09	
$(CH_3)_2NCHO$	1.47	1.54	1.53	1.60	1.79	1.84	1.88	1.89
C_6H_5CN			1.76	1.77	1.83	1.90	1.98	1.97

[a] 5% solutions. [b] Value at 80°.

Table VI. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of 2,6-Dichlorophenylacetaldehyde

Solvent[a]	J_{HH}, Hz									
	-30°	-15°	0°	15°	38°	60°	90°	120°	140°	160°
cyclohexane				1.13	1.19	1.23	1.27[b]			
trans-decalin	.90	.98	1.12	1.13	1.22	1.24	1.28	1.35	1.35	1.35
CCl_4		1.05	1.10	1.10	1.18	1.24				
$(CH_3CH_2)_2O$	.87	.98	1.03	1.02	1.14					
THF	.70	.85	.88	.95	1.04	1.09				
$CHCl_3$	.99	1.02	1.05	1.09	1.19					
CH_2Br_2	.82	.93	.98	1.08	1.15	1.20	1.27			
CH_2Cl_2	.79	.91	.96	.96	1.10					
$(CH_3)_2CO$	.52	.65	.69	.76	.90					
$(CH_3)_2NCHO$			.56	.62	.76	.86	.97	1.05		
C_6H_5CN			.77	.82	.97	1.02	1.08	1.18		

[a]5% solutions. [b]Value at 80°.

Table VII. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant of Phenylmercaptoacetaldehyde

Solvent[a]	J_{HH}, Hz							
	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane				3.37	3.28	3.18	3.09[b]	
trans-decalin	3.36	3.37	3.28	3.29	3.27	3.18	3.06	2.94
$(CH_3CH_2)_2O$	3.29	3.34	3.19	3.18	3.15			
THF	3.09	3.15	3.06	3.02	3.00	2.95		
CH_2Br_2	3.24	3.25	3.13	3.17	3.17	3.03	3.00	
$(CH_3)_2NCHO$	2.79	2.82	2.77	2.80	2.77	2.73	2.75	
C_6H_5CN			2.98	2.92	2.93	2.87	2.84	2.79

[a] 5% solutions. [b] Value at 80°.

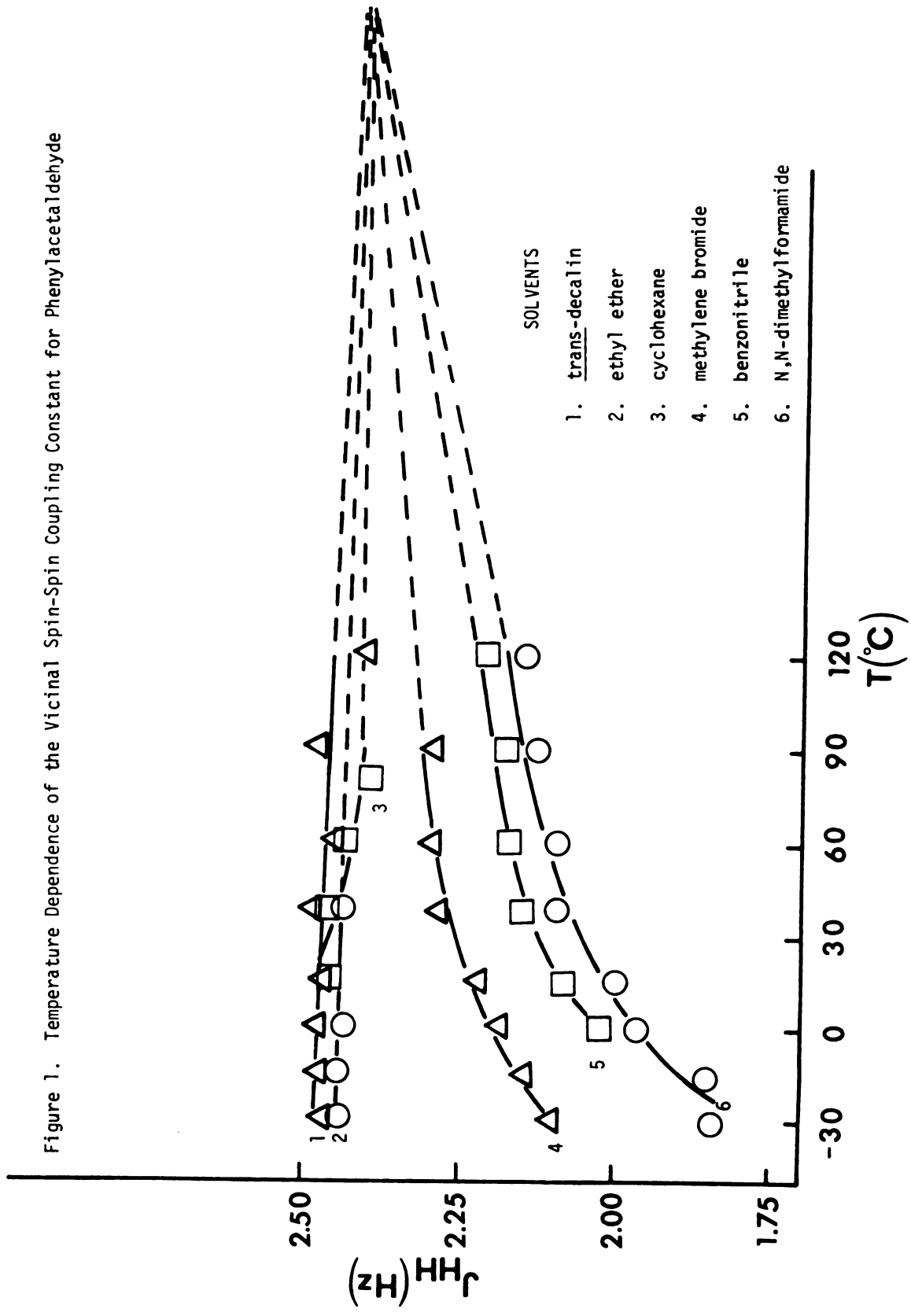


Figure 1. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for Phenylacetaldehyde

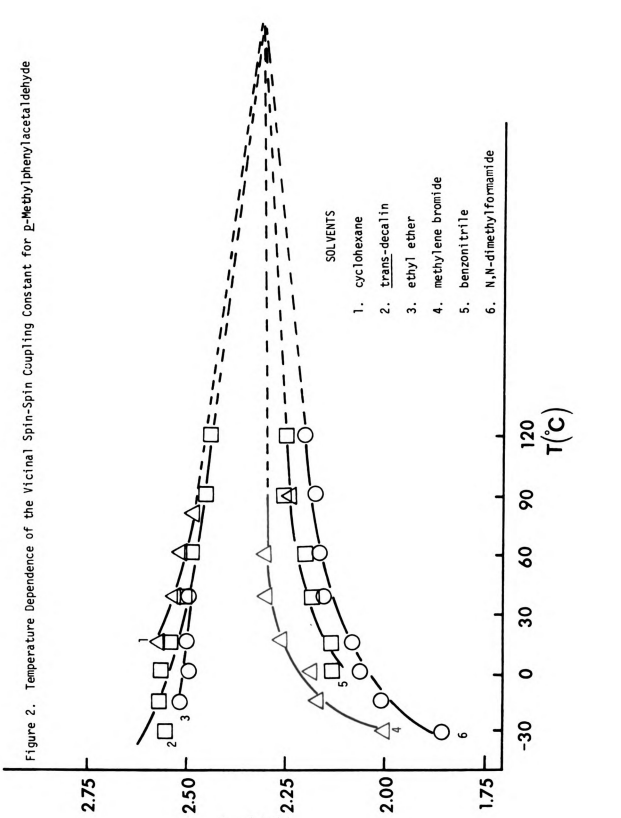


Figure 2. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for p-Methylphenylacetaldehyde

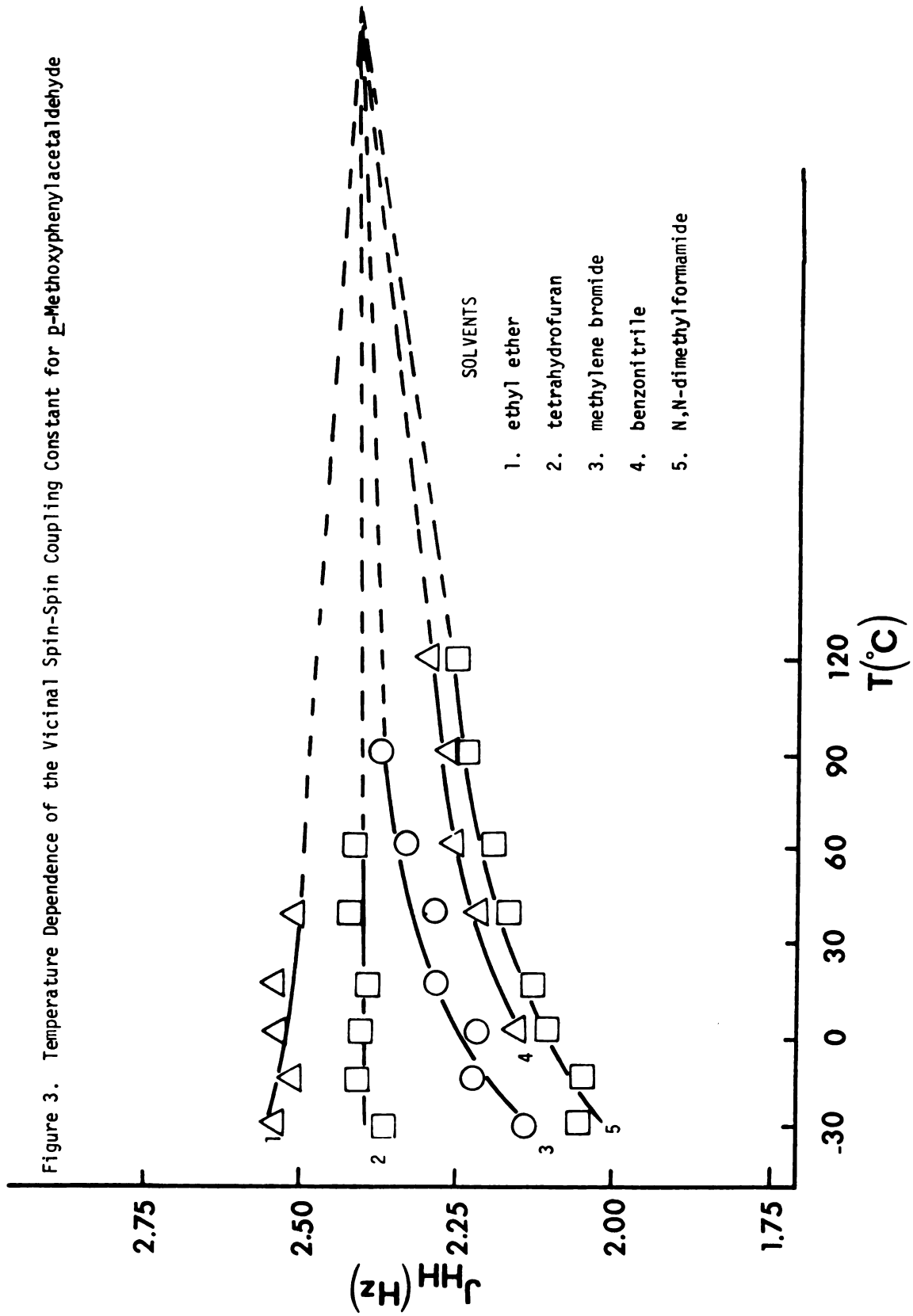


Figure 3. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for p-Methoxyphenylacetaldehyde

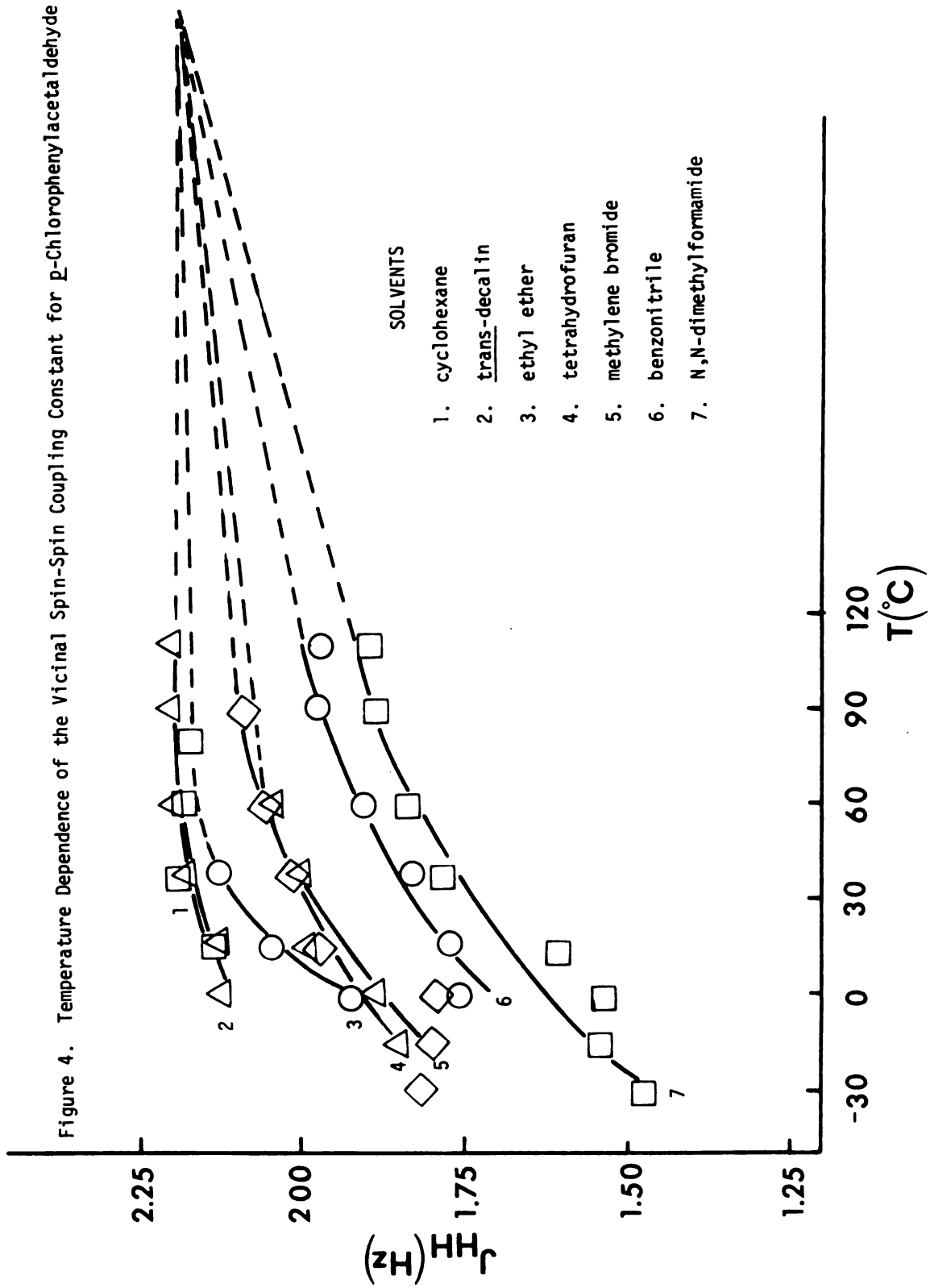


Figure 4. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for p-Chlorophenylacetaldehyde

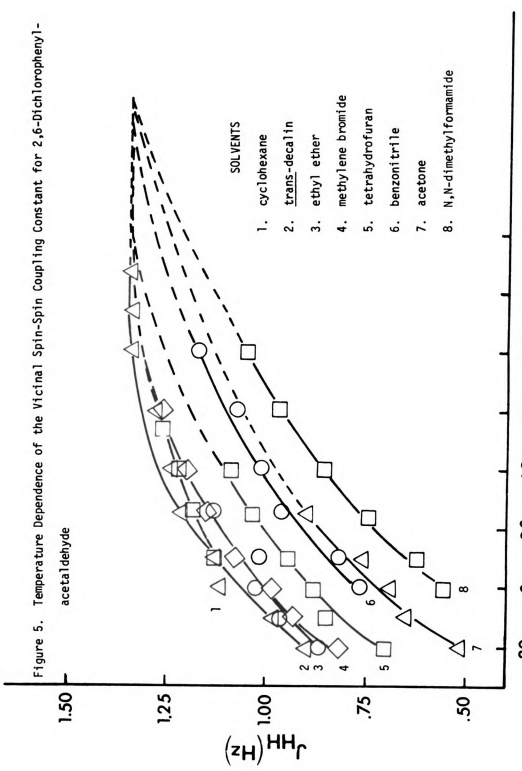
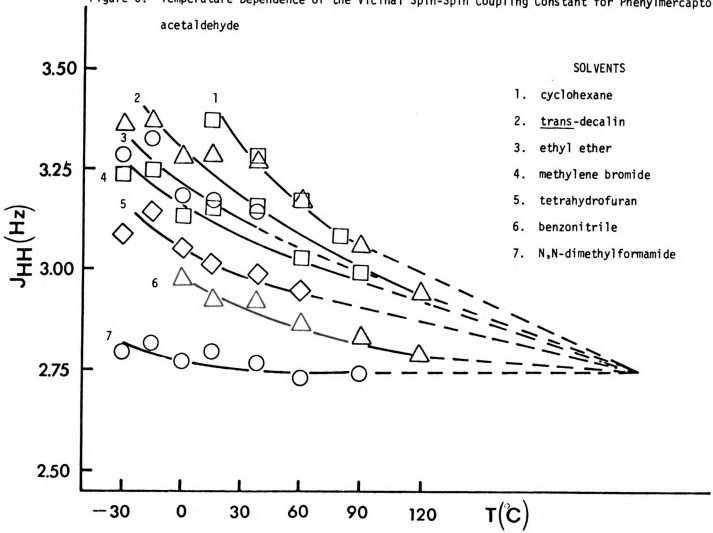


Figure 5. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for 2,6-Dichlorophenylacetaldehyde

Figure 6. Temperature Dependence of the Vicinal Spin-Spin Coupling Constant for Phenylmercapto-acetaldehyde



trends are noted in the case of p-methylphenylacetaldehyde, Fig. 2, the coupling constant becoming temperature independent at a value of 2.30 Hz. In p-methoxyphenylacetaldehyde, the coupling constant remained constant in ethyl ether and tetrahydrofuran, but increased with increasing temperature in methylene bromide, dimethyl formamide, and benzonitrile. It also becomes temperature independent at a value of 2.40 Hz as seen in Fig. 3. The coupling constants for p-chlorophenylacetaldehyde and 2,6-dichlorophenylacetaldehyde increased with increasing temperature in all solvents studied. The coupling constant of p-chlorophenylacetaldehyde appears to become temperature independent at 2.20 Hz as shown in Fig. 4. The coupling constant for 2,6-dichlorophenylacetaldehyde is considerably smaller than those of the other phenylacetaldehydes and appears to become temperature independent at 1.35 Hz as shown in Fig. 5. The coupling constant for phenylmercaptoacetaldehyde decreased with increasing temperature in all solvents studied, except in dimethyl formamide, where it remained constant. The coupling becomes temperature independent at 2.75 Hz, Fig. 6.

B. Chemical Shifts

Summarized in Table VIII are the solvent dependencies of the chemical shifts of the aldehydic and methylenic protons of the substituted phenylacetaldehydes and phenylmercaptoacetaldehyde. The chemical shifts were measured in 5% (vol./vol. for liquids or wt./wt. for solids) solutions using tetramethylsilane as an internal standard. The values were calibrated at a sweep width of 1000 Hz using a known sample of tetramethylsilane (0.0 Hz), cyclohexane (86.0 Hz), acetone (126.7 Hz), 1,1,1-trichloroethane (164.0 Hz), dioxane (217.0 Hz), methylene chloride (318.0 Hz), and chloroform (439.8 Hz).

Table VIII. Solvent Dependence of the Chemical Shifts[a] of Substituted Phenylacetaldehydes and Phenylmercaptoacetaldehyde

	$PhCH_2CHO$		p-CH_3PhCH_2CHO		p-CH_3OPhCH_2CHO		p-$ClPhCH_2CHO$		2,6-Cl_2PhCH_2CHO		$PhSCH_2CHO$	
Solvent[b]	H_1[c]	H_2[d]	H_1[c]	H_2[d]	H_1[c]	H_2[d]	H_1[c]	H_2[d]	H_1[c]	H_2[d]	H_1[c]	H_2[d]
cyclohexane	578	207	577	205			573	207	575	238	567	200
trans-decalin	576	208	576	205			576	208	576	238	566	201
$(CH_3CH_2)_2O$	579		578		576		581		581		570	
THF					577		580		578		570	
CH_2Br_2	589	225	587	220	583	218	586	223	585		576	219
$(CH_3)_2CO$									586	248		
$(CH_3)_2NCHO$	585	227	586	224	583	221[e]	589	232	589		580	
C_6H_5CN	585	220	588	219	584	217	588	222[e]	583	241	574	220

[a]TMS as internal reference. [b]5% solutions at 38°. [c]Chemical shift of the aldehydic proton. [d]Chemical shift of the methylenic proton. [e]Value at 15°.

The chemical shifts of the aldehydic and methylenic protons moved to lower fields as the solvent polarity increased. Those of the methylenic protons, however, underwent a much larger change than those of the aldehydic proton in all compounds studied, except 2,6-dichlorophenylacetaldehyde.

The temperature dependence of the chemical shifts of the phenylacetaldehydes is given in Tables IX, X, XI, XII, and XIII. With increasing temperature, the chemical shifts of the methylenic protons of the para-substituted phenylacetaldehydes remained constant or were shifted downfield in solvents of low dielectric constant and upfield in those of high dielectric constant. The chemical shifts of the aldehydic protons remained constant or were shifted downfield with increasing temperature. For 2,6-dichlorophenylacetaldehyde, the chemical shifts of the methylenic protons and of the aldehydic proton were shifted upfield with increasing temperature, regardless of solvent dielectric constant.

The temperature dependence of the chemical shifts of phenylmercaptoacetaldehyde is given in Table XIV. With increasing temperature, the chemical shift of the methylenic protons moved downfield in solvents of low dielectric constant and upfield in those of high dielectric constant. The chemical shift of the aldehydic proton remained constant or was shifted downfield with increasing temperature.

Table IX. Temperature Dependence of the Chemical Shifts of Phenylacetaldehyde[a]

Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane								
CHO				574	578	581	582[c]	
CH_2				206	207	208	209[c]	
trans-decalin								
CHO	566	568	570	570	576	576	581	585
CH_2	204	206	205	205	208	207	209	210
$(CH_3CH_2)_2O$								
CHO	572	574	575	576	579			
CH_2								
CH_2Br_2								
CHO	579	581	584	584	589	585	588	
CH_2	223	221	222	222	225	220	220	
$(CH_3)_2NCHO$								
CHO	581	583	584	585	585	585	591	593
CH_2	229	231	229		227	226	228	226
C_6H_5CN								
CHO			584	586	585	583	589	591
CH_2			222	223	220	217	220	219

[a]TMS as internal reference. [b]5% solutions. [c]Value at 80°.

Table X. Temperature Dependence of the Chemical Shifts of p-Methylphenylacetaldehyde[a]

Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane								
CHO				573	577	580	581[c]	
CH_2				204	205	206	207[c]	
trans-decalin								
CHO	561	566	569	572	576	578	580	584
CH_2	200	202	203	204	205	206	206	208
$(CH_3CH_2)_2O$								
CHO	571	573	574	575	578			
CH_2								
CH_2Br_2								
CHO	577	579	581	583	587	587	589	
CH_2	219	219	220	219	220	219	219	
$(CH_3)_2NCHO$								
CHO	577	580	582	583	586	587	587	592
CH_2	225	224			224	223	222	223
C_6H_5CN								
CHO			584	585	588	587	589	591
CH_2			219	219	219	217	217	217

[a]TMS as internal standard. [b]5% solutions. [c]Value at 80°.

Table XI. Temperature Dependence of the Chemical Shifts of p-Methoxyphenylacetaldehyde[a]

Solvent	-30°	-15°	0°	15°	38°	60°	90°	120°
$(CH_3CH_2)_2O$								
CHO	571	572	573		576			
CH_2								
THF								
CHO	571	569	572	574	577	576		
CH_2								
CH_2Br_2								
CHO	581	581	581	585	583	583	582	
CH_2	220	221	218	221	218	216	216	
$(CH_3)_2NCHO$								
CHO	580	578	580	581	583	582	582	582
CH_2				221		220	218	218
C_6H_5CN								
CHO			583	585	584	584	583	581
CH_2					217	216	214	212

[a]TMS as internal reference. [b]5% solutions.

Table XII. Temperature Dependence of the Chemical Shifts of p-Chlorophenylacetaldehyde[a]

Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane								
CHO				572	573	577	576[c]	
CH_2				205	207	207	206[c]	
trans-decalin								
CHO			573	572	576	577	576	576
CH_2			209	207	208	207	209	207
$(CH_3CH_2)_2O$								
CHO		578	577	578	581			
CH_2								
THF								
CHO	582	576	572	580	580	582		
CH_2								

Table XII. (Continued)

Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°
CH_2Br_2								
CHO	586	586	582	585	586	586	587	
CH_2	223		221	222	223	221	219	
$(CH_3)_2NCHO$								
CHO	589	588	585	589	589	588	586	585
CH_2				232	232	228	226	
C_6H_5CN								
CHO			585	587	588	588	587	584
CH_2			223	222		220	220	216

[a]TMS as internal standard. [b]5% solutions. [c]Value at 80°.

Table XIII. Temperature Dependence of the Chemical Shifts of 2,6-Dichlorophenylacetaldehyde [a]

Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°	140°	160°
cyclohexane										
CHO				575	575	575	574[c]			
CH_2				238	238	237	237[c]			
trans-decalin										
CHO	575	576	574	575	576	575	575	572	573	569
CH_2	238	237	238	238	238	237	235	235	235	234
CCl_4										
CHO		578	575	579	579	577				
CH_2		242	240	240	240	239				
$(CH_3CH_2)_2O$										
CHO	582	582	580	580	581					
CH_2										
TMF										
CHO	582	582	579	580	578	577				
CH_2										
$CHCl_3$										
CHO	587	584	580	583	582					
CH_2	247		245	245	244					

Table XIII. (Continued)

Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°	140°	160°
CH_2Br_2										
CHO	590	588	586	586	585	584	579			
CH_2							242			
CH_2Cl_2										
CHO	589	585	581	578	581					
CH_2			246							
$(CH_3)_2CO$										
CHO	590	590	588	588	586					
CH_2	255	254	252	252	248					
$(CH_3)_2NCHO$										
CHO	596	594	592	592	589	588	585	584		
CH_2								248		
C_6H_5CN										
CHO			586	584	583	582	580	578		
CH_2			242	241	241	241	240	239		

[a]TMS as internal standard. [b]5% solutions. [c]Value at 80°.

Table XIV. Temperature Dependence of the Chemical Shifts of Phenylmercaptoacetaldehyde[a]

Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°
cyclohexane								
CHO				561	567	567	567[c]	
CH_2				199	200	201	201[c]	
trans-decalin								
CHO	561	561	561	562	566	567	567	567
CH_2	199	201	200	200	201	201	202	201
$(CH_3CH_2)_2O$								
CHO	566	566	565	564	570			
CH_2								
THF								
CHO	565	564	565	565	570	570		
CH_2								

Table XIV. (Continued)

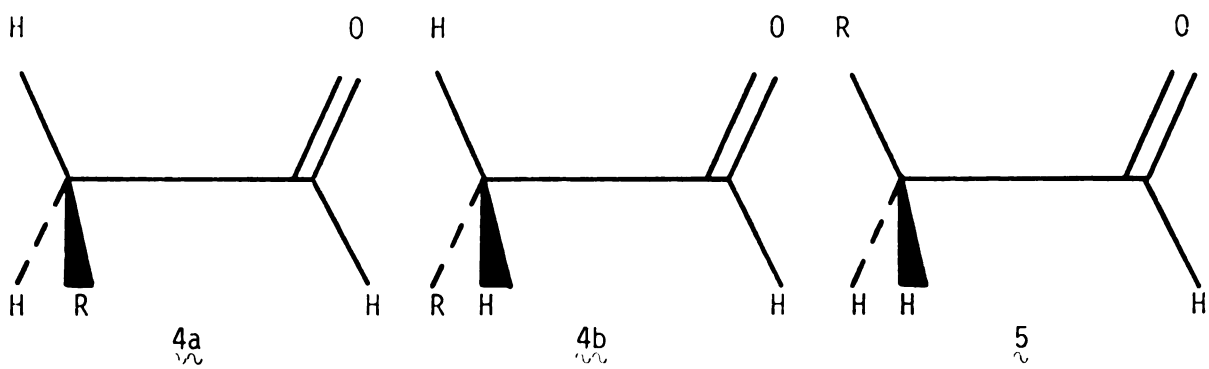
Solvent[b]	-30°	-15°	0°	15°	38°	60°	90°	120°
CH_2Br_2								
CHO	573	571	573	573	576	576	575	
CH_2	220	219	221	217	219	218	217	
$(CH_3)_2NCHO$								
CHO	575	574	574	574	580	575	578	
CH_2	239	238	237	235		235	231	
C_6H_5CN								
CHO			575	575	574	577	575	575
CH_2			222	221	220	219	217	215

[a]TMS as internal reference. [b]5% solutions. [c]Value at 80°.

DISCUSSION

A. Spin-Spin Coupling Constants

The data in Tables I, II, III, IV, V, VI, and VII have been interpreted in terms of an equilibrium between rotamers 4 and 5. It is assumed that $J_t > J_g$, where J_t is the trans coupling constant and J_g is the gauche. The observed coupling constant would be temperature independent if 4a, 4b, and 5 were isoenergetic. If 4a were more stable



than 5, the observed vicinal coupling constant would decrease with increasing temperature; conversely, it would increase with increasing temperature if 4a were less stable than 5. The following conclusions can be drawn from the temperature dependence of the spin-spin coupling constants of the aldehydes investigated: 1) The rotamers of phenylacetaldehyde are isoenergetic (i.e., no change in the observed coupling with temperature) in solvents of low dielectric constant. However, in solvents of high dielectric constant, the most stable rotamer is 5. 2) In solvents of low dielectric constant, rotamer 4a of p-methylphenyl-

acetaldehyde is more stable than 5. In solvents of intermediate dielectric constant, such as ethyl ether and tetrahydrofuran, 4a and 5 are isoenergetic. In solvents of high dielectric constant, 5 is the more stable rotamer. 3) For p-methoxyphenylacetaldehyde, 4a and 5 are isoenergetic in ethyl ether and tetrahydrofuran, while 5 is more stable in solvents of high dielectric constant. 4) For p-chlorophenylacetaldehyde in cyclohexane or trans-decalin, 4a and 5 are isoenergetic at or above 38°, but in solvents of higher dielectric constant, 5 is more stable than 4a. 5) For 2,6-dichlorophenylacetaldehyde, 5 is more stable than 4a in all solvents studied. 6) For phenylmercaptoacetaldehyde, 4a is more stable than 5 except in dimethyl formamide where they are isoenergetic.

Rotamer populations were calculated using equation 1, where J_{obsd}

$$J_{obsd} = p(J_t + J_g)/2 + (1-p)J_g \qquad (1)$$

is the observed coupling constant, p is the fractional population of 4 (4a + 4b), and (1-p) that of 5. Free energy differences, $\Delta G°$, between 4a and 5 were calculated from equation 2. The enthalpy

$$\Delta G° = -RT\ln(J_t + J_g - 2J_{obsd})/(J_{obsd} - J_g) \qquad (2)$$

differences, $\Delta H°$, between 4a and 5 were obtained from plots of log K_{eq} versus 1/T, where K_{eq} is the equilibrium constant given by equation 3.

$$K_{eq} = 2(1-p)/p \qquad (3)$$

For the above calculations, the values of J_t and J_g must be known or estimated. For systems with large changes in J_{obsd}, limits for J_t and J_g may be set using equation 4, which relates the experimental

$$J_{obsd} = (1/3)(J_t + 2J_g) \qquad (4)$$

coupling constant to J_t and J_g, either when the rotamers are equally populated, or at free rotation about the carbon-carbon single bond (usually at very high temperatures).

In cases, such as those investigated here, where the changes in J_{obsd} are relatively small, such estimates are not easily made. Since J_t and J_g for acetaldehyde have been estimated (27) as 7.6 and 0.5 Hz, respectively, the temperature independent value of the coupling constant can be used to estimate the correction needed to be applied to the observed couplings to allow the use of J_t and J_g of acetaldehyde in equations 1 and 2. The temperature independent values for phenylacetaldehyde, p-methylphenylacetaldehyde, p-methoxyphenylacetaldehyde, p-chlorophenylacetaldehyde, 2,6-dichlorophenylacetaldehyde, and phenylmercaptoacetaldehyde are 2.40, 2.30, 2.40, 2.20, 1.35, and 2.75 Hz, respectively. Using a value of 2.85 Hz for the coupling constant of acetaldehyde, the applied corrections are +0.45, +0.55, +0.45, +0.65, +1.50, and +0.10 Hz, respectively.

Using the above method, the effect of the solvent dielectric constant on the relative populations of $\underset{\sim}{4}$ and $\underset{\sim}{5}$ for the substituted phenylacetaldehydes studied was determined. The results of these calculations are given in Table XV. Since the temperature independent coupling constants for p-chloro- and 2,6-dichlorophenylacetaldehyde are lower than those usually found for monosubstituted aldehydes, the calculations for these compounds were also performed as if the temperature independent coupling constants for both were 2.40 Hz. As noted previously from the coupling constant data, the population of $\underset{\sim}{5}$ increases as the solvent dielectric constant increases. This same effect can be seen in Table XVI in terms of the free energy differences, $\Delta G°$, calculated from equation 2. The enthalpy differences ($\Delta H°$)

Table XV. Solvent Dependence of the Relative Rotamer Populations[a] of Substituted Phenylacetaldehydes

Solvent	$PhCH_2CHO$	p-CH_3PhCH_2CHO	p-CH_3OPhCH_2CHO	p-$ClPhCH_2CHO$		2,6-Cl_2PhCH_2CHO	
	%ξ	%ξ	%ξ	%ξ		%ξ	
				A[b]	B[c]	A[d]	B[c]
cyclohexane	32	28		34	39	38	68
trans-decalin	32	28		34	40	37	67
$(CH_3CH_2)_2O$	33	28	31	36	41	40	69
THF	36		33	39	45	42	72
CH_2Br_2	37	34	37	39	44	39	69
$(CH_3)_2CO$						46	77
$(CH_3)_2NCHO$	43	38	41	45	51	50	80
C_6H_5CN	41	38	39	44	50	44	74

[a]All values calculated for 5% solutions at 38°. [b]J_{obsd} = 2.20 Hz. [c]J_{obsd} = 2.40 Hz. [d]J_{obsd} = 1.35 Hz.

Table XVI. Solvent Dependence of the Free Energy Differences[a], $\Delta G°$, Between Rotamers of Substituted Phenylacetaldehydes

Solvent	$PhCH_2CHO$ $\Delta G°$, cal/mole, for 4a ⇄ 5	p-CH_3PhCH_2CHO $\Delta G°$, cal/mole, for 4a ⇄ 5	p-CH_3OPhCH_2CHO $\Delta G°$, cal/mole, for 4a ⇄ 5	p-$ClPhCH_2CHO$ $\Delta G°$, cal/mole, for 4a ⇄ 5		2,6-Cl_2PhCH_2CHO $\Delta G°$, cal/mole, for 4a ⇄ 5	
				A[b]	B[c]	A[d]	B[c]
cyclohexane	+40	+170		-20	-155	-125	-900
trans-decalin	+50	+150		-20	-180	-100	-870
$(CH_3CH_2)_2O$	+10	+150	+70	-75	-205	-180	-930
THF	-70		+10	-155	-305	-230	-1020
CH_2Br_2	-110	-20	-100	-155	-280	-155	-930
$(CH_3)_2CO$						-330	-1185
$(CH_3)_2NCHO$	-240	-130	-210	-305	-455	-430	-1295
C_6H_5CN	-210	-110	-150	-280	-430	-280	-1080

[a]These values were calculated from the corresponding data at 38° in Table XV. [b]J_{obsd} = 2.20 Hz. [c]J_{obsd} = 2.40 Hz. [d]J_{obsd} = 1.35 Hz.

between 4 and 5, determined from reasonably linear plots of log K_{eq} versus 1/T, are given in Table XVII. The effect of solvent dielectric constant on the relative populations of 4 and 5 for phenylmercaptoacetaldehyde are given in Table XVIII. The free energy differences, $\Delta G°$, and the enthalpy differences, $\Delta H°$, between 4 and 5 are given in Table XIX.

The relative stabilities of rotamer 5 compared with 4a for the monosubstituted acetaldehydes studied here and previously (27,28,30) are:

$$R = CH_3 > CH_3CH_2 \sim OC_6H_5 \sim OCH_3 > CH(CH_3)_2 > Cl > 2,6\text{-}(Cl)_2C_6H_3 \sim \underline{p}\text{-}ClC_6H_4 \geq C_6H_5 \sim \underline{p}\text{-}CH_3OC_6H_4 \sim \underline{p}\text{-}CH_3C_6H_4 \sim Br > C(CH_3)_3 > SCH_3 \sim SC_6H_5$$

This order is only valid in solvents of low dielectric constant, such as cyclohexane or trans-decalin. In solvents of high dielectric constant, the methoxy, phenoxy, chloro, and bromo groups become more effective than the methyl group in the above order. The position of the more polarizable methylmercapto group with respect to that of the less polarizable methoxy group, along with that of bromine with respect to chlorine, has been used to show that dipole-induced dipole interactions play only a minor role in determining the relative stabilities of 4 and 5 (30). Nonbonded repulsions are partly responsible for the positions of the bulky t-butyl and methylmercapto groups. However, their relative positions (30) reinforce the conclusion (27) that nonbonded repulsions are not the overriding factor controlling rotamer stability. From the great similarity in $\Delta G°$ and $\Delta H°$ values between the para-substituted phenylacetaldehydes in a given solvent, it appears that overall dipole-dipole interactions are not a major factor determining rotamer stability, but rather only local dipole-dipole interactions are important. Since the $\Delta G°$ and $\Delta H°$ values for 2,6-dichlorophenylacetaldehyde are more

Table XVII. Solvent Dependence of the Enthalpy Differences[a], $\Delta H°$, Between Rotamers of Substituted Phenylacetaldehydes

Solvent	$PhCH_2CHO$ $\Delta H°$, cal/mole, for 4a ⇄ 5	p-CH_3PhCH_2CHO $\Delta H°$, cal/mole, for 4a ⇄ 5	p-CH_3OPhCH_2CHO $\Delta H°$, cal/mole, for 4a ⇄ 5	p-$ClPhCH_2CHO$ $\Delta H°$, cal/mole, for 4a ⇄ 5		2,6-Cl_2PhCH_2CHO $\Delta H°$, cal/mole, for 4a ⇄ 5	
				A[b]	B[c]	A[d]	B[c]
cyclohexane	+220	+350		0	0	-535	-535
trans-decalin	0	+280		0	-175	-565	-760
$(CH_3CH_2)_2O$	0	0	0	-1100	-1050	-630	-930
THF			0	-620	-515	-890	-940
CH_2Br_2	-420	-430	-360	-700	-650	-790	-850
$(CH_3)_2CO$						-940	-1500
$(CH_3)_2NCHO$	-520	-340	-350	-715	-900	-1020	-1655
C_6H_5CN	-360	-310	-370	-665	-500	-830	-1135

[a]These values were obtained by plotting the natural logarithm of the equilibrium constants calculated from the rotamer populations versus 1/T. [b]J_{obsd} = 2.20 Hz. [c]J_{obsd} = 2.40 Hz. [d]J_{obsd} = 1.35 Hz.

Table XVIII. Solvent Dependence of the Relative Rotamer Populations[a] of Phenylmercaptoacetaldehyde

Solvent	$PhSCH_2CHO$ %5
cyclohexane	19
trans-decalin	19
$(CH_3CH_2)_2O$	22
THF	27
CH_2Br_2	22
$(CH_3)_2NCHO$	33
C_6H_5CN	29

[a]All values calculated for 5% solutions at 38°.

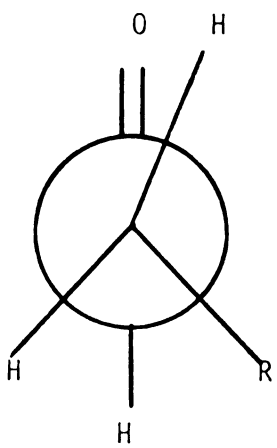
Table XIX. Solvent Dependence of the Free Energy Difference[a], $\Delta G°$, and the Enthalpy Difference[b], $\Delta H°$, Between Rotamers of Phenylmercaptoacetaldehyde

Solvent	$PhSCH_2CHO$ $\Delta G°$, cal/mole, for 4a ⇄ 5	$PhSCH_2CHO$ $\Delta H°$, cal/mole, for 4a ⇄ 5
cyclohexane	+415	+1670
trans-decalin	+415	+1050
$(CH_3CH_2)_2O$	+310	+540
THF	+165	+440
CH_2Br_2	+310	+660
$(CH_3)_2NCHO$	+10	+100
C_6H_5CN	+110	+500

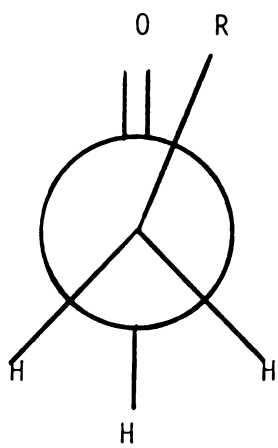
[a]These values were calculated from the corresponding data at 38° in Table XVIII. [b]These values were obtained by plotting the natural logarithm of the equilibrium constants calculated from the rotamer populations versus 1/T.

negative than for the para-substituted phenylacetaldehydes, overall dipole-dipole interactions are probably not important; and this difference may be due to attractive interactions between the chloro and the carbonyl groups.

For p-chloro- and 2,6-dichlorophenylacetaldehyde, the rotamer populations, $\Delta G°$, and $\Delta H°$ were also calculated as if the temperature independent value of J_{obsd} were 2.40 Hz. Although $\Delta G°$ values are sensitive to J_{obsd}, $\Delta H°$ values are less so. There appears to be no reason to assume that all the compounds studied should have the same temperature independent value. If rotamers 8 and 9 are considered, the temperature independent value of J_{obsd} is a function of the energy wells for the rotamers of the system. If the energy wells for 8 and 9



8

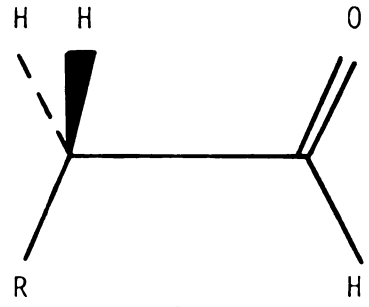


9

are broad, then J_{obsd} will become temperature independent at lower temperatures (accessible to experimental measurement) than if the reverse were true. Thus, the temperature independent values of J_{obsd} may have different values due to the effect of the substituents on the shape of the energy wells describing the system.

The possibility of a twofold barrier to rotation may be eliminated by considering rotamers 5 and 10 as the equilibrium conformations. The

relevant vicinal spin-spin coupling constants would be J_g (60°) from 5



10

and $J_{120°}$ from 10. For a twofold barrier to rotation, equation 4 becomes equation 4'. From the observed coupling constants, J_g must be equal

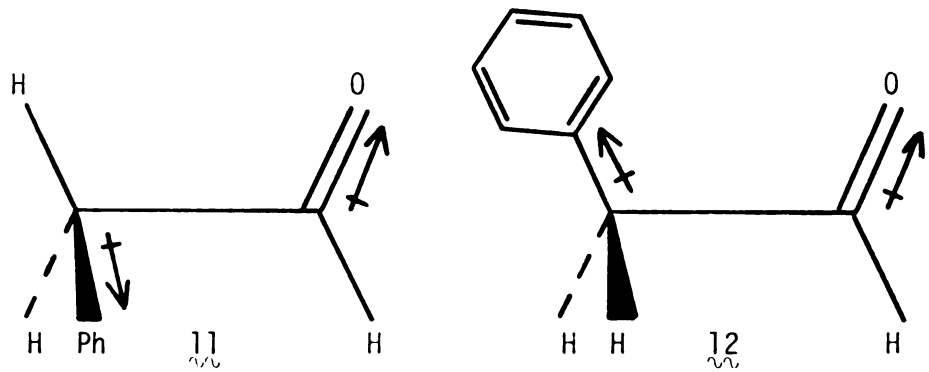
$$J_{obsd} = (1/2)(J_g + J_{120°}) \qquad (4')$$

to or smaller than 1.84, 1.85, 2.05, 1.47, and 0.52 Hz for phenyl-, p-methylphenyl-, p-methoxyphenyl-, p-chlorophenyl-, and 2,6-dichlorophenylacetaldehyde, respectively. If J_g and $J_{120°}$ are assumed to be of the same sign, then $J_{120°}$ would be equal to or greater than 2.96, 2.76, 2.74, 2.92, and 2.48 Hz, respectively. These results are unreasonable, since J_g and $J_{120°}$ are expected to have similar values (32,38). Since J_g for all these compounds is certainly less than 1 Hz, the discrepancy between J_g and $J_{120°}$ is even greater than that calculated using the minimum values of the observed coupling constants. If J_g and $J_{120°}$ are assumed to be of opposite sign, the discrepancy is larger than if the coupling constants are assumed to have the same sign.

B. The Effect of Solvent Polarity on Rotamer Stabilities

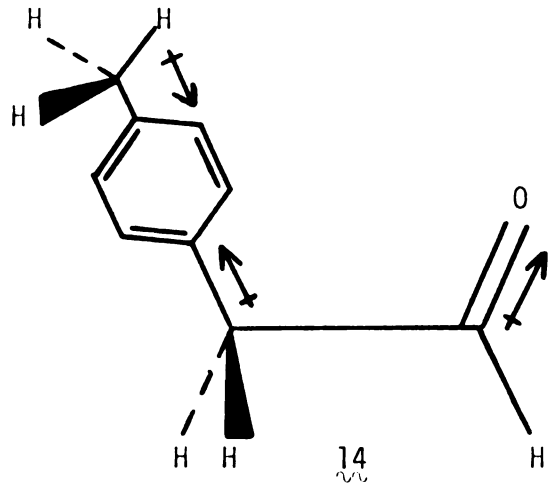
The increase in the rotamer ratio 5/4 for phenylacetaldehyde with increasing solvent dielectric constant, as reflected in the populations given in Table XV, is logical in light of the higher dipole moment of 5

relative to 4 (illustrated by 11 and 12).



11 12

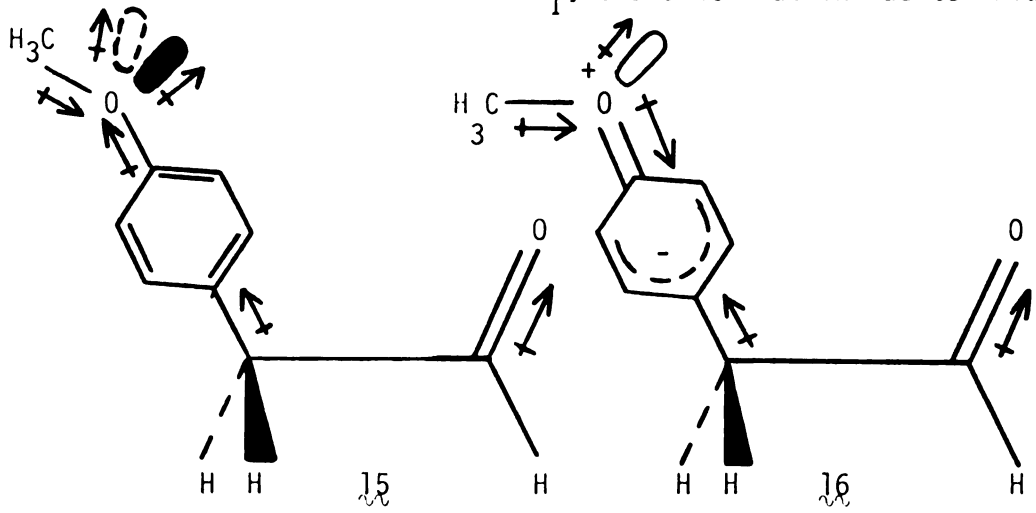
In the case of p-methylphenylacetaldehyde, the dipoles may be represented as in 14. It is apparent that the dipoles, other than the carbonyl, should almost completely cancel. If, therefore, overall



14

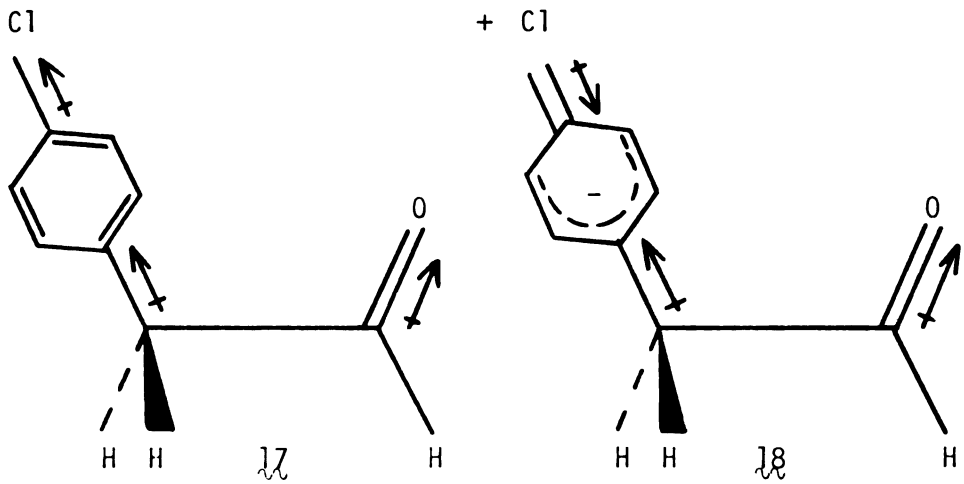
dipole-dipole interactions are important in determining rotamer stability, then the rotamer populations of 4 and 5 should remain constant for p-methylphenylacetaldehyde regardless of solvent dielectric constant. This is not the case. The populations of 4 and 5 (and the free energy and enthalpy differences) are roughly equivalent to and change in the same manner as those of phenylacetaldehyde, supporting the idea that only local dipole-dipole interactions are important in determining rotamer stability.

In p-methoxyphenylacetaldehyde, the overall dipole will depend on the relative importance of the charge separated resonance form, 16, to 15. Taft and coworkers (39) have taken σ_p values for the ionization of benzoic acids and the rate of saponification of benzoate esters and estimated the contributions of σ_I, the contribution due to induction,



and σ_R, the contribution due to resonance. Taft's values of σ_I and σ_R indicate that the methoxy group withdraws electrons by induction and donates electrons by resonance, the resonance contribution being about twice as large as the inductive. Comparison of the dipole moments for anisole, 1.16 D (40), chlorobenzene, 1.52 D (41), bromobenzene, 1.51 D (42), p-chloroanisole, 2.24 D (43), and p-bromoanisole, 2.23 D (44) also indicates that the dipole arising from the methoxy group is directed towards the phenyl group. This would indicate that rotamer 4 has a higher overall dipole moment than 5 in p-methoxyphenylacetaldehyde; consequently 4 should increase in stability relative to 5 in going to solvents of higher dielectric constant if overall dipole-dipole interactions are important. This is not the case; rather, the observed trends for rotamer populations, free energy differences, and enthalpy differences are similar to those of phenylacetaldehyde. This again implies that local dipole-dipole interactions are important in determining rotamer stability.

In the case of p-chlorophenylacetaldehyde, two resonance forms, 17 and 18, are again possible. Taft's σ_I and σ_R values (39) indicate

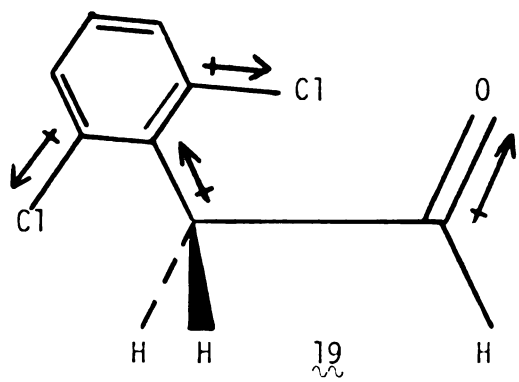


17 18

that the inductive withdrawal of electrons is about twice as important as the resonance effect. Comparison of the dipole moments for chlorobenzene, 1.52 D (41), nitrobenzene, 3.84 D (45), toluene, 0.4 D (41), p-chloronitrobenzene, 2.55 D (40), and p-chlorotoluene, 1.74 D (46) shows that the dipole due to the chloro group is directed away from the phenyl group. It would be predicted, if overall dipole moment were important, that the percentage of 5 for p-chlorophenylacetaldehyde should be greater than for phenyl-, p-methylphenyl-, or p-methoxyphenylacetaldehyde in solvents of high dielectric constant. This is not the case. The populations, free energy differences, and enthalpy differences are again similar to those of phenylacetaldehyde. These results are again consistent with local dipole-dipole interactions being the major factor determining rotamer stability.

The important dipoles for 2,6-dichlorophenylacetaldehyde are shown in 19. If the overall dipole moment were important, then in solvents of high dielectric constant, rotamer 5 should be less stable for the dichloro compound than for phenylacetaldehyde. This is not the

case. In proceeding from nonpolar to polar solvents, the change in



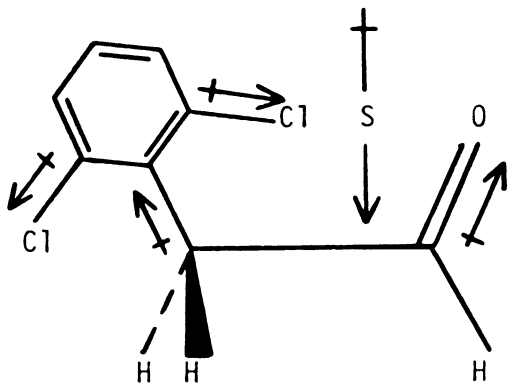
19

populations is about the same as for phenylacetaldehyde. If the populations for 4 and 5 are similar to those calculated using 2.40 Hz as the temperature independent value of the coupling constant, then the larger population of 5 for 2,6-dichlorophenylacetaldehyde to that of phenylacetaldehyde must be explained by some other factor than local dipole-dipole interactions. Such a factor could be an attractive interaction between chlorine and oxygen. In any event, the overall dipole-dipole interactions cannot be of major importance.

The results for phenylmercaptoacetaldehyde may be compared to those previously obtained for methylmercaptoacetaldehyde (30). It is found that the magnitude and trends in rotamer populations, free energy differences, and enthalpy differences are the same. This may be due to the dominance of local dipole-dipole interactions or due to the steric effect of sulfur. If, however, overall dipole-dipole interactions were of major importance, some difference between the phenylmercapto- and methylmercaptoacetaldehyde would have been expected due to the polarizability of sulfur.

The above results and discussion indicate that local dipole-dipole interactions are important in determining rotamer stability, while overall dipole-dipole interactions are of minor importance.

A close examination of the data in Table VI shows that the coupling constant of 2,6-dichlorophenylacetaldehyde decreases in going to solvents of higher dielectric constant, but for the more bulky polar solvents within the series (chloroform, methylene bromide, and methylene chloride) an increase in the coupling constant may be due to a coordination of the bulky solvent, S, as in 20, which would destabilize rotamer 5 due to steric interactions with the chlorines.



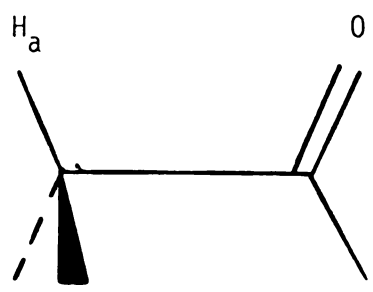
20

In comparing the $\Delta H°$ and $\Delta G°$ values, it should be remembered that $\Delta H°$ in high dielectric constant solvents may be overly negative, since the dielectric constant of the solvent decreases as the temperature increases. This decrease in the dielectric constant causes a decrease in the rotamer ratio, 5/4, and results in the calculation of more negative $\Delta H°$ values. For this reason, in solvents of high dielectric constant, $\Delta G°$ values generally reflect the enthalpy difference to a better degree than do the $\Delta H°$ values themselves. This change in dielectric constant with temperature becomes a severe problem in systems where rotamer dipole moments differ greatly. In the aldehydes studied, however, $\Delta G°$ and $\Delta H°$ are usually the same within experimental error indicating that $\Delta S°$ is probably zero. For p-chlorophenylacetaldehyde there is a discrepancy between $\Delta G°$ and $\Delta H°$, indicating that $\Delta S°$ may

not be zero. The $\Delta G°$ and $\Delta H°$ values calculated for 2,6-dichlorophenylacetaldehyde, using 1.35 Hz as the temperature independent value of the coupling constant, indicate that $\Delta S°$ may be close to zero for solvents of low dielectric constant, but not so for those of high dielectric constant. Using 2.40 Hz gives $\Delta G°$ and $\Delta H°$ values of roughly the same value, indicating that $\Delta S°$ may be nearly zero in all solvents if this temperature independent value is valid.

C. Chemical Shifts

The chemical shift data for the substituted phenylacetaldehydes may be interpreted best by using model 7 (36) rather than model 6 (35). Model 6 would predict that H_a in 21 would be deshielded in the plane



21

of the carbonyl group, while 7 would predict it to be shielded. From Table VIII, it can be seen that for nonaromatic solvents, the chemical shifts of the methylenic protons move upfield as the dielectric constant of the solvent decreases. Therefore, these protons are being shielded to a greater extent than in solvents of high dielectric constant. The previous results on rotamer stability show that for the substituted phenylacetaldehydes the stability of rotamer 4 is increased as the solvent dielectric constant is decreased. Therefore, the methylenic protons are being shielded as predicted by model 7. The

same arguments may be applied to the chemical shifts of phenylmercapto-acetaldehyde.

The temperature dependence of the chemical shifts of the aldehydic and methylenic protons for the substituted phenylacetaldehydes are given in Tables IX, X, XI, XII, and XIII. It is seen that as the population of rotamer 4 increases, the chemical shifts of the methylenic protons move upfield, a fact that is consistent with model 7. The aldehydic protons for phenylacetaldehyde, p-methylphenylacetaldehyde, and p-methoxyphenylacetaldehyde were deshielded with increasing temperature in all the solvents studied. The chemical shift of the aldehydic proton for p-chlorophenylacetaldehyde was deshielded in solvents of low dielectric constant and remained relatively constant in solvents of high dielectric constant with increasing temperature. The aldehydic proton in 2,6-dichloroacetaldehyde was shielded with increasing temperature in all solvents studied. The reasons for this behavior of the aldehydic protons is not presently understood.

The temperature dependence of the chemical shifts for the aldehydic and methylenic protons for phenylmercaptoacetaldehyde are given in Table XIV. The chemical shift of the methylenic protons in most solvents was constant. In N,N-dimethylformamide and benzonitrile, the methylenic protons are deshielded with increasing population of rotamer 4. This may be due to specific solvent solute interactions. The aldehydic proton was deshielded with increasing temperature in less polar solvents and was constant in polar solvents.

EXPERIMENTAL

A. Reagents and Compounds

All aldehydes were purified either by distillation or by isolation of the bisulfite addition product. Phenylacetaldehyde, p-methylbenzyl cyanide, 2-methyl-2,4-pentanediol, p-methoxystyrene, p-chlorostyrene, 2,6-dichlorostyrene, chloroacetaldehyde diethyl acetal, and benzenethiol were obtained commercially (Aldrich Chemical Co.).

B. Solvents

All solvents used in these studies were purified by standard methods (47). The purified solvents were stored over molecular sieves in glass stoppered bottles.

C. Synthesis

I. p-Methylphenylacetaldehyde

p-Methylphenylacetaldehyde was prepared from p-methylbenzyl cyanide by combining the procedures of Tillmanns and Ritter (48) and Meyers, et al. (49). To 90 g of concentrated sulfuric acid cooled in an ice bath, was added 25 g of p-methylbenzyl cyanide (0.19 mole) with stirring over a period of 0.5 hours, followed by 21.3 g of 2-methyl-2,4-pentanediol (0.18 mole) added over a two hour period. This mixture was poured over 180 g of ice, half-neutralized with 40% sodium hydroxide solution and extracted three times with 100 ml of chloroform. The pH was then adjusted to 10 and the product was extracted with ethyl ether and dried over anhydrous potassium carbonate. After evaporation of the

ether extracts, 8.5 g of 2-(p-methylbenzyl)-4,4,6-trimethyl-5,6-dihydro-1,3(4H)-oxazine (19.6%) was obtained as a yellow oil which solidified on distillation (84-90° at 0.3 mm). The product was dissolved in a mixture of 200 ml of tetrahydrofuran and 200 ml of 95% ethanol, cooled to -40° and 9N HCl and sodium borohydride solution (7.6 g, in 15 ml of water containing 2 drops of 40% sodium hydroxide) were added alternately, keeping the pH between 6 and 8. The reaction mixture was cooled for an additional two hours, 200 ml of water was added and the solution was made basic with 40% sodium hydroxide. The layers were separated and the aqueous layer extracted twice with ethyl ether. The combined organic layers were washed twice with 200 ml of saturated sodium chloride solution and dried over anhydrous potassium carbonate. After evaporation of the solvent, the crude 2-(p-methylbenzyl)-4,4,6-trimethyltetrahydro-1,3-oxazine was added dropwise to 300 ml of water containing 100 g of oxalic acid. The produced aldehyde was steam distilled under a helium atmosphere. The distillate was saturated with sodium chloride and extracted three times with 150 ml portions of pentane. Distillation of the dried pentane extracts yielded 1.6 g of pure p-methylphenylacetaldehyde (0.011 mole, 6.6%, 44-46° at 0.5 mm).

II. p-Methoxyphenylacetaldehyde

p-Methoxyphenylacetaldehyde was prepared from p-methoxystyrene by the procedure of Mannich and Jacobsohn (50). To a suspension of 22 g of yellow mercuric oxide in a solution of 10 g of p-methoxystyrene (0.74 mole), 100 ml of ethyl ether and 10 ml of water, was added small portions of iodine (25 g) over a period of one hour. The solution was filtered and washed twice with saturated sodium thiosulfate solution. The solution was diluted with 50 ml of ethanol. After the removal of ether and addition of 100 ml of saturated sodium bisulfite, the solution

was stirred for one hour and the bisulfite adduct was filtered and washed with ethyl ether. After addition of 100 ml of saturated sodium bicarbonate to an aqueous solution of the adduct, the solution was stirred for one hour at 0° and then extracted with ethyl ether, dried over anhydrous sodium sulfate and evaporated to give 3.9 g of p-methoxyphenylacetaldehyde (0.026 mole, 35%).

III. p-Chlorophenylacetaldehyde

p-Chlorophenylacetaldehyde was prepared from p-chlorostyrene by the procedure of Freeman et al. (51,52,53). To 10 g (0.0725 mole) of freshly distilled p-chlorostyrene dissolved in 250 ml of methylene chloride and cooled to 0° was added dropwise 12.6 g (6.6 ml, 0.082 mole) of freshly distilled chromyl chloride dissolved in 125 ml of methylene chloride. After one hour, 6.10 g (0.094 mole) of zinc dust was added. It was followed, after an additional 15 minutes of stirring, by 37 ml of water and 15 g of ice. The mixture was allowed to reach room temperature and then steam distilled until 5 ℓ of distillate were collected. The distillate was extracted with an equal volume of methylene chloride, the organic layer was dried over anhydrous magnesium sulfate, decanted, and the solvent evaporated. The resulting oil was distilled, yielding 0.48 g (0.0031 mole, 4.3%) of p-chlorophenylacetaldehyde (colorless solid, bp 75-78 at 0.6 mm).

IV. 2,6-Dichlorophenylacetaldehyde

2,6-Dichlorophenylacetaldehyde was prepared from 2,6-dichlorostyrene by the procedure of Freeman et al. (51,52,53). To a stirred mixture of 10.30 g (0.059 mole) of freshly distilled 2,6-dichlorostyrene in 200 ml of methylene chloride and cooled to 0° was added dropwise 10.32 g (5.4 ml, 0.067 mole) of freshly distilled chromyl chloride

dissolved in 100 ml of methylene chloride. An hour later, 5 g (0.077 mole) of zinc dust was added, followed, after an additional 15 minutes of stirring, by 30 ml of water and 12 g of ice. The mixture was allowed to reach room temperature and then steam distilled until 5 ℓ of distillate were collected. The distillate was extracted with an equal volume of methylene chloride, the organic layer was dried over anhydrous magnesium sulfate, decanted, and the solvent evaporated. The resulting oil was distilled, yielding 1.45 g (0.0077 mole, 12.9%) of 2,6-dichlorophenylacetaldehyde (colorless solid, bp 95-98° at 0.2 mm).

V. Phenylmercaptoacetaldehyde

Phenylmercaptoacetaldehyde was prepared from benzenethiol and chloroacetaldehyde diethyl acetal by the procedure of Wick, et al. (54). To a solution of sodium phenylmercaptide (11.0 g, 0.48 mole, of sodium, 120 ml of ethanol, 58.3 g, 0.53 mole, of benzenethiol) chilled in an ice bath was added dropwise 39.65 g (0.26 mole) of chloroacetaldehyde diethyl acetal. After warming, the mixture was heated at 50-60° for one hour, and was then allowed to stand at room temperature overnight. The resulting orange solution containing a white solid was filtered, and the filtrate was diluted with water to twice its volume and extracted with ether. The ether layer was dried with anhydrous magnesium sulfate. After evaporation of the ether and vacuum distillation of the residue 32.16 g of phenylmercaptoacetaldehyde diethyl acetal (0.14 mole, 54.2%, 131-35° at 3.4 mm) was obtained.

A mixture of 22.6 g (0.1 mole) of phenylmercaptoacetaldehyde diethyl acetal and 120 ml of 10% sulfuric acid was refluxed at 80° for 45 minutes. The mixture was then steam distilled and the distillate extracted with ether. The ether layer was dried with anhydrous magnesium

sulfate and the ether evaporated. Vacuum distillation gave 5.45 g of phenylmercaptoacetaldehyde (0.036 mole, 36.0%, 108-110° at 3.7 mm).

D. N.M.R. Spectra

The Nuclear Magnetic Resonance spectra were obtained at 60 MHz on a Varian Associates Model A56/60D Analytical Spectrometer (Varian Associates, Palo Alto, Calif.). Samples, in concentrations of 5% vol./vol. for liquids or wt./wt. for solids, were run with tetramethylsilane (TMS) as the internal standard. Coupling constants (J) were recorded at a sweep width of 50 Hz. The recorded coupling constants were averages of six to ten measurements and were calibrated against known values of acetaldehyde (26,37). Chemical shifts were obtained at a sweep width of 1000 Hz and were calibrated against a known sample of tetramethylsilane (0.0 Hz), 1,1,1-trichloroethane (164.0 Hz), dioxane (217.0 Hz), methylene chloride (318.0 Hz), and chloroform (439.8 Hz). Temperature studies were carried out by using a Varian Associates V-6040 Variable Temperature controller with a precision of $\pm 2°$.

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