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Intramolecular Hydrogen Bonding in α-Keto and α-Alkoxy Carboxylic Acids. VIII. *o*-Methoxy-Substituted Phenoxyacetic and Phenylthioacetic Acids

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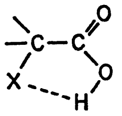
The infrared spectra in the O–H stretching region of several *ortho*-substituted phenoxyacetic and phenylthioacetic acids were determined in dilute carbon tetrachloride solutions. The O–H stretching absorption of phenoxyacetic acids carrying *o*-methoxy-substituents shows three absorption maxima, all of these being attributed to the monomeric species, and they are assigned to the free O–H group, the O–H group hydrogen bonded with α-phenoxy oxygen atom and the O–H group hydrogen bonded with methoxyl oxygen atom in the order of decreasing frequency. The O–H stretching absorption at the lower frequency of *o*-methoxyphenylthioacetic acids is also assigned to the hydrogen bonded monomeric species in which the chelation occurs between the carboxylic O–H group and the methoxyl oxygen atom.

From the previous investigations of the present authors,[1–9] the existence, as well as the steric and electronic behaviors, of the intramolecular hydrogen bonding (shown in (**1**)) in some carboxylic acids has become definite. The conclusion of these investigations shows (i) that only the acids with α-alkoxy groups ($n=1$) can form intramolecular hydrogen bonds in the homologous sereis RO(CH$_2$)$_n$COOH, and (ii) that the occurrence of the hydrogen bonding is limited only when the hydrogen accepting group is an alkoxy, aryloxy, or oxo group.

In this paper, the intramolecular hydrogen bonding of the titled compounds is discussed, and it is shown that the methoxy groups at the *ortho* positions of phenoxyacetic and phenylthioacetic acids can participate as hydrogen acceptors in the COOH···O hydrogen bonding.



(**1**)

Expreimental

Preparation of Materials. All phenols employed in the preparation of phenoxyacetic acids are known and were prepared by the methods described previously.[10] Substituted phenoxyacetic acids were prepared either by the condensation of the phenol with chloroacetic acid in strongly alkaline aqueous medium,[11] or by the action of ethyl chloroacetate on the sodium phenoxide without the presence of solvents[12] followed by saponification. The following phenoxyacetic acids (shown in Table 1) were thus prepared and used in the further investigations. Most of the benzenethiols were prepared from the corresponding anilines by the action of potassium ethylxanthate,[13] and the others by the reduction of the corresponding benzenesulfonyl chlorides.[14] The phenylthioacetic acids were prepared by the methods similar to those of phenoxyacetic acids. The physical properties and the elementary analyses are shown in Table 2. Phenylpropionic acids and other materials were either prepared by the methods described or purchased commercial products, and used after appropriate purification.

Measurement of Infrared Spectra. The infrared spectra were recorded on a Perkin Elmer 112G grating infrared spectrophotometer in the O–H stretching region. The measurement was carried out in a carbon tetrachloride solution at a concentration less than 0.002 mol/l. The dimeric association of the carboxylic acids were not significant in this concentration range. To distinguish the absorption bands due to the dimer from those of the monomer, the concentration dependences of their absorption intensities were also measured with some typical acids.

The wave numbers, the extinction coefficients, and the halfwidths of the overlapping bands were obtained by the least square calculations employing an NEAC 2230 computer.

Results and Discussion

The O–H stretching spectra are listed in Table 3 for phenoxyacetic acids, in Table 4 for phenylthioacetic acids and in Table 5 for some related compounds, and some typical spectra were illustrated in Figs. 1 and 2.

The intramolecular hydrogen bonding in aryloxyacetic acids without *ortho* substituent has been studied by the present authors,[2–5] and it has been shown that the acids have two absorptions in the O–H stretching region. The envelope of each absorption band could be approximated with the Lorentz function within experimental errors. The typical of them is phenoxyacetic acid (Fig. 1a) which has two O–H stretching absorptions at 3527 cm^{-1} and 3488 cm^{-1}. These absorptions are assigned to the free monomeric form **2** and intramolec-

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[1] M. Ōki and M. Hirota, This Bulletin, **33**, 119 (1960).

[2] M. Ōki and M. Hirota, *ibid.*, **34**, 374 (1961).

[3] M. Ōki and M. Hirota, *ibid.*, **34**, 378 (1961).

[4] M. Ōki and M. Hirota, *Spectrochim. Acta*, **17**, 583 (1961).

[5] M. Ōki and M. Hirota, This Bulletin, **36**, 290 (1963).

[6] M. Ōki and M. Hirota, *ibid.*, **37**, 209 (1964).

[7] M. Ōki and M. Hirota, *ibid.*, **37**, 213 (1964).

[8] M. Ōki, M. Hirota, and S. Hirofuji, *Sepctrochim. Acta*, **22**, 1537 (1966).

[9] M. Ōki and M. Hirota, *Nippon Kagaku Zasshi*, **86**, 115 (1965).

[10] a) R. C. Huston and M. M. Ballard, "Organic Syntheses," Coll. Vol. II, p. 97 (1943); b) T. Mazima and Y. Okazaki, *Ber.*, **49**, (1916); c) Kalle & Co., D. R. P. 95337, 16721 (1945).

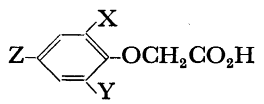
[11] P. Fritzsche, *J. Prakt. Chem.*, [2] **20**, 269 (1879).

[12] J. Grundy, *J. Chem. Soc.*, **1954**, 2649.

[13] C. M. Sutar and H. L. Hansen, *J. Amer. Chem. Soc.*, **54**, 4102 (1932).

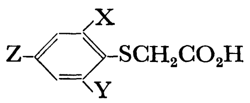
[14] R. Adams, "Organic Syntheses," Coll. Vol. I, p. 504 (1941).

Table 1. Phenoxyacetic acids.



Substituents			Melting points (°C)		Analyses			
					Found		Calcd	
X	Y	Z	Obsd	Lit	C(%)	H(%)	C(%)	H(%)
H	H	H	98.2	98				
CH_3	H	H	153.5	153				
Cl	H	H	146.5	146				
Br	H	H	140.3	143				
Br	H	CH_3	142.7		44.23	3.72	44.11	3.70
Br	Br	CH_3	175.9		33.51	2.39	33.37	2.49
Br	CH_3	CH_3	150.5		46.08	4.25	46.35	4.28
NO_2	H	H	156.4	156.5				
CH_3	CH_3	H	137.5		66.75	6.65	66.65	6.71
OCH_3	H	H	121.5	129	59.34	5.72	59.33	5.53
OCH_3	CH_3	H	102					
OCH_3	Br	CH_3	129.5		43.42	4.00	43.66	4.03
OC_6H_5	H	H	100.0		68.73	4.97	68.84	4.95

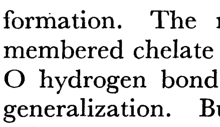
Table 2. Phenylthioacetic acids.



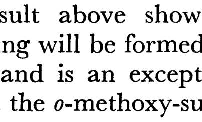
Substituents			Melting points (°C)		Analyses			
					Found		Calcd	
X	Y	Z	Obsd	Lit	C(%)	H(%)	C(%)	H(%)
H	H	H	61.7	62				
H	H	CH_3	75.1		59.50	5.57	59.33	5.53
OCH_3	H	H	118.1		54.76	5.27	54.53	5.09
OCH_3	OCH_3	H	88.5		52.75	5.39	52.62	5.30
Br	H	CH_3	119.3		41.60	3.69	41.39	3.47
Br	Br	CH_3	135.1		32.02	2.45	31.80	2.37

ularly hydrogen bonded monomeric form **3**, respectively. The O–H absorptions of *ortho*-substituted phenoxyacetic acids are essentially the same as the unsubstituted ones when the *ortho*-substituents are not hydrogen acceptors. Thus, *o*-methylphenoxyacetic acid has two absorptions at 3529 and 3485 cm^{-1} attributable to the free and hydrogen bonded monomeric forms, respectively.

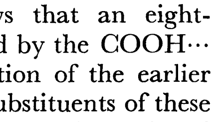
However, a third absorption band (band IV of *ortho*-methoxy-derivatives) is observed when the *ortho*-substituent can act as hydrogen acceptor. The bands IV of *o*-methoxy-substituted acids appear at frequencies between 3400 and 3300 cm^{-1} and their halfwidths $\Delta\nu_{1/2}$, about 100 cm^{-1}, are by far larger than the absorption bands I and II. The *o*-methoxyphenylthioacetic acids also absorb at about 3330 cm^{-1} (as exemplified by the absorption band at 3352 cm^{-1} of *o*-methoxyphenylthioacetic acid (No. 16) and the one at 3333 cm^{-1} of 2,6-dimethoxyphenylthioacetic acid (No. 17)) and the halfwidths of these absorption bands are again near 100 cm^{-1}. Thus, the bands IV of *o*-methoxy substituted phenoxyacetic acids and the bands at the similar frequencies of *o*-methoxy-substituted phenylthioacetic acids might be absorption bands caused by the same kind of molecular interaction. The arylthioacetic acid without *o*-methoxy groups has only one absorption band attributable to the free monomeric form in the O–H stretching region. As the absorption has been assigned to the monomeric species the only plausible assignment for the band at a lower frequency is that it arises from the carboxylic hydroxyl group intramolecularly hydrogen bonded to the oxygen atom of the *o*-methoxyl group.



(**2**)



(**3**)



(**4**)

The authors have concluded that the existence of the COOH···O hydrogen bond of alkoxy- or aryloxy-acetic acid was limited to the case in which the acid forms a five-membered chelate ring by the hydrogen bond formation. The result above shows that an eight-membered chelate ring will be formed by the COOH···O hydrogen bond, and is an exception of the earlier generalization. But the *o*-methoxy-substituents of these acids are located at a close distance from the carboxyl

Table 3. The O–H stretching absorptions of substituted phenoxyacetic acids in dilute carbon tetrachloride solutions

No.	Substituents			i	$\nu_{\max}$ (cm^{-1})	$\varepsilon_{\max}$	$\Delta\nu_{1/2}$	A$\times 10^{-3}$ (l/mol cm^2)	A$_i$/A$_\text{I}$	A$_\text{IV}$/A$_\text{II}$	$\Delta\nu_{\max}$ (cm^{-1})
	X	Y	Z								
1	H	H	H	I	3527	49.5	31.7	5.68			
				II	3488	25.1	29.7	2.70	0.48		39
2	Me	H	H	I	3529	49.0	33.1	5.87			
				II	3485	24.0	33.9	2.94	0.50		43
3	Cl	H	H	I	3529	47.6	30.3	5.22			
				II	3480	47.5	47.3	8.13	1.56		49
4	NO_2	H	H	I	3525	—[a]	29.2	—			
				II	3430	—[a]	101.0	—	4.46		95
5	Me	Me	H	I	3530	44.4	31.3	5.03			
				II	3457	75.0	39.6	10.7	2.14		73
6	OMe	H	H	I	3527	46.0	33.8	5.63			
				II	3463	69.1	39.5	9.87	1.75		64
				IV	3355	51.6	116.9	21.8	6.97	2.21	172
7	OMe	Me	H	I	3532	18.5	28.7	1.94			
				II	3453	56.0	49.7	10.1	5.24		79
				III	3406	13.6	42.9	2.11	1.10		126
				IV	3318	67.1	131.9	32.0	16.6	3.18	214
8	OMe	Br	Me	I	3531	14.6	40.8	2.16			
				II	3454	77.0	57.6	16.0	7.44		77
				III	3417	17.1	38.6	2.39	1.11		114
				IV	3350	68.4	102.6	25.4	11.8	1.58	181
9	OC_6H_5	H	H	I	3530	29.4	30.2	3.21			
				II	3461	45.0	47.8	7.78	2.42		69
				IV	3395	24.0	82.0	7.12	2.22	0.92	135

a) Measured in a saturated solution

Table 4. The O–H stretching absorptions of substituted phenylthioacetic acids in dilute carbon tetrachloride solutions

No.	Substituents				$\nu_{\max}$ (cm^{-1})	$\varepsilon_{\max}$	$\Delta\nu_{1/2}$	A$\times 10^3$ (l/mol cm^2)	A$_\text{b}$/A$_\text{f}$	$\Delta\nu_{\max}$ (cm^{-1})
	X	Y	Z							
10	H	H	H	f	3528	61.5	33.6	7.48		
11	H	H	Me	f	3527	60.0	29.7	6.45		
12	OMe	H	H	f	3530	53.5	27.5	5.30		
				b	3352	21.5	122.0	9.49	1.79	178
13	OMe	OMe	H	f	3533	29.5	28.6	3.05		
				b	3333	77.2	85.6	23.9	7.83	200
14	Br	H	Me	f	3527	65.7	29.6	7.04		
15	Br	Br	Me	f	3529	69.8	24.2	6.11		

Table 5. The O–H stretching absorptions of some related acids

Acid	$\nu_{\max}$ (cm^{-1})	$\varepsilon_{\max}$	$\Delta\nu_{1/2}$ (cm^{-1})	A$\times 10^{-3}$ (l/mol cm^2)
cis-o-Methoxycinnamic	3537	77.1	27.4	7.64
trans-o-Methoxycinnamic	3543	65.7	26.2	6.21
β-(*o*-Methoxyphenyl)-propionic	3534	64.9	21.7	5.08
β-Phenylpropionic	3532	59.4	24.0	2.24

group when the molecule takes a suitable conformation, and the hydrogen bond formation is not so unusual if the hydrogen bonding is mainly controlled by the steric accessibility of the donor hydroxyl group and an oxygen acceptor.

The fact that the band IV arises from the unassociated monomeric species is verified by the measurement of the concentration dependence of the O–H spectra carried out with some of these acids. An example is shown in Fig. 3 in which the O–H spectrum of 2,6-dimethoxyphenylthioacetic acid is illustrated at three different concentrations. In Fig. 3, the molar extinction coefficients of both the 3533 cm^{-1} band (band I) and the 3333 cm^{-1} band (band IV) increase as the concentration decreases. The increase in intensity can be interpreted that the monomeric species is more favorable at lower concentrations. The absorption due to the dimer lies in the frequency range between 3200 and 2500 cm^{-1}, and the isosbestic point near 3275 cm^{-1} indicates the

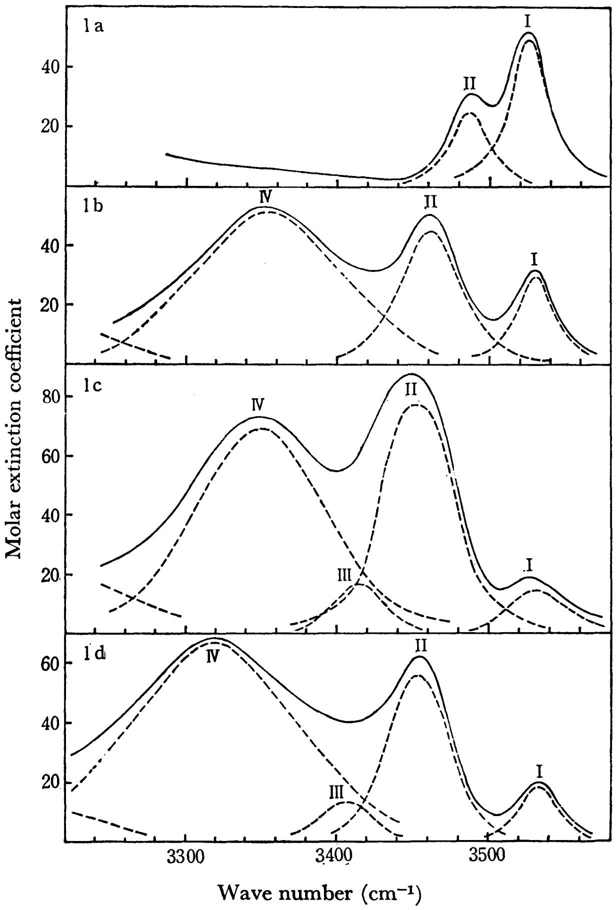


Fig. 1. The O–H Stretching Absorptions of *p*-Methoxyphenoxyacetic Acids in dilute Carbon Tetrachloride Solution.
1a: Phenoxyacetic Acid,
1b: 2-Methoxyphenoxyacetic Acid,
1c: 2-Methoxy-4-methyl-6-bromophenoxyacetic Acid and
1d: 2-Methoxy-6-methylphenoxyacetic Acid

existence of the monomer-dimer equilibrium.[15]

To determine the extent of the existence of the $COOH\cdots OCH_3$ hydrogen bond of this type, the O–H stretching absorptions of *o*-methoxy-substituted β-phenylpropionic and *cis*-cinnamic acids were observed, and the absence of the $COOH\cdots OCH_3$ hydrogen bond was concluded because no absorption bands other than the free monomeric species appear in the O–H stretching region (as shown in Table 5).

The ultraviolet spectral studies on *cis*-cinnamic acids show that their aromatic rings and ethylenic linkages do not lie in the same plane, and angles between the two chromophores are estimated to be about 40° by comparison of the absorption intensities of the *cis* and the *trans* isomers.[16] In *cis*-*o*-methoxycinnamic acid, a much larger angle between the aryl and the ethylenic groups is expected from is lower intensity in π-π^* transition, though the calculation of the exact value for this angle is meaningless because the approximation does not hold in a case of such large steric hindrance.[17] Anyhow, the deviation of the aryl ring from the planar conformation increases the distance between the *o*-methoxy and the carboxyl groups in *cis*-*o*-methoxycinnamic acid and makes it difficult to form the intramolecular hydrogen bond.

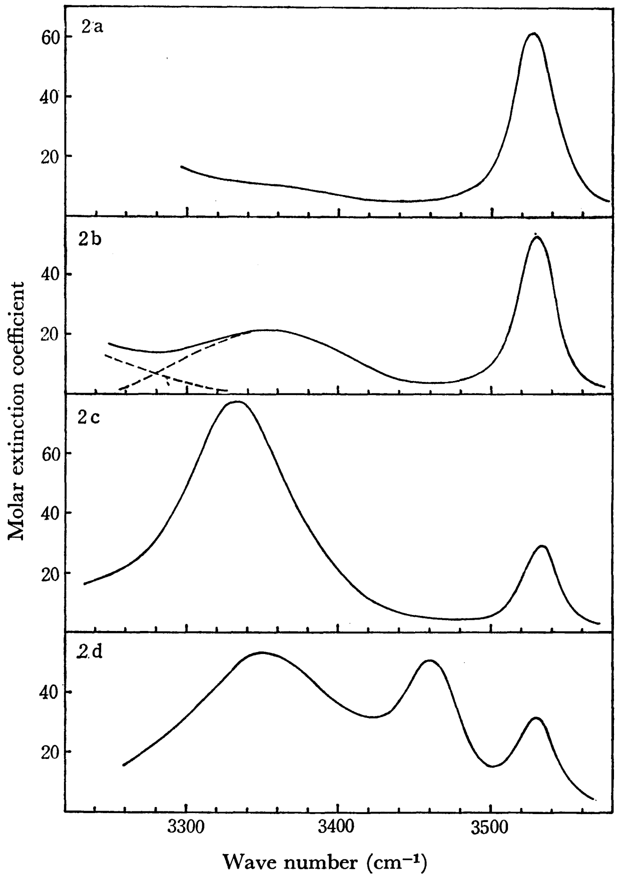


Fig. 2. The O–H Stretching Absorptions of *o*-Methoxyphenylthioacetic Acids in Dilute Carbon Tetrachloride Solution.
2a: Phenylthioacetic Acid,
2b: 2-Methoxyphenylthioacetic acid,
2c: 2,6-Dimethoxyphenylthioacetic Acid and
2d: 2-Methoxyphenoxyacetic Acid (for Comparison)

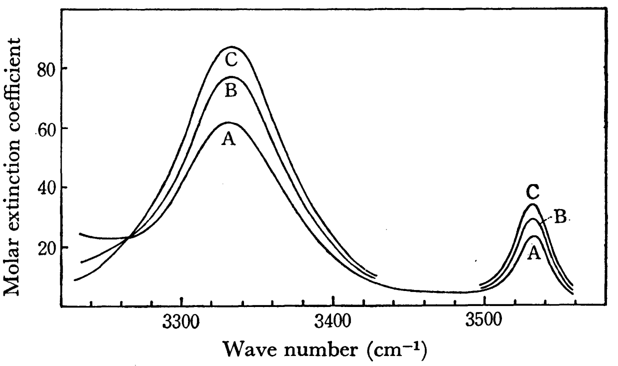


Fig. 3. Concentration Dependence of the O–H Absorption Bands of 2,6-Dimethoxyphenylthioacetic Acid. Spectra A, B, and C are measured in carbon tetrachloride at concentrations 3.048×10^{-3}, 1.016×10^{-3}, and 5.08×10^{-4} mol/*l*, respectively.

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[15] The measurement of the infrared spectra was carried out at a concentration less than 0.002 mol/*l* in order to lessen the effect of concentration. Nevertheless, the absolute values of the intensity are less significant quantities than their ratios.

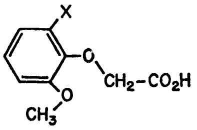
[16] Y. Urushibara and M. Hirota, *Nippon Kagaku Zasshi*, **82**, 354–358 (1961).

[17] E. A. Braude and F. Sondheimer, *J. Chem. Soc.*, **1955**, 3754.

The absence of the intramolecular hydrogen bond in β-(*o*-methoxyphenyl)propionic acid is explained in the following way. Difference in conformation between aryloxyacetic acids and β-aryloxypropionic acids may arise from the absence of the β-hydrogen atoms and aryl-oxygen conjugation in the former compound. The former factor restricts the conformations of the rotamers about the C_β-C_α bond of the β-arylpropionic acid, and may affect unfavorably on the hydrogen bond formation. The aryl-oxygen conjugation in phenoxy group enforces the essentially planar Ar–O–C conformation (either (**5**) or (**6**)) to the *o*-methoxyphenoxyacetic acid.[18] Thus the carboxyl group is located in the neighborhood of the *o*-methoxyl group in the conformation (**5**). The freedom of the rotation about the phenyl-β-carbon bond in β-aryloxypropionic acid may act as an entropically unfavorable factor to the hydrogen bond formation.

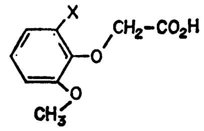
The other fact to be interpreted is why the intramolecular hydrogen bond is present in *o*-methoxyphenoxyacetic acid while it is absent in β-methoxypropionic acid.[1] The presence of the eight-membered intramolecular hydrogen bond is understood if the carboxyl group can form hydrogen bond maintaining the energetically favorable *cis*[19]-conformation (which is about 2 kcal/mol more stable than the *trans*).[20] The β-methoxypropionic acid should take the *trans*[19] conformation to form the intramolecular hydrogen bond. The *cis* conformation of the carboxyl group is very probable from the spectral data of the same compounds in the carbonyl stretching region.

The integrated intensity ratio A_{IV}/A_I corresponds to the ratio of the $COOH\cdots OCH_3$ hydrogen bonded species to the free monomeric species, which represents how favorable the hydrogen bonded conformation is, and $\Delta\nu$ is assumed to be linear with the energy of hydrogen bond formation.[21] The parallel relation between the A_{IV}/A_I and $\Delta\nu$ is observed with the *o*-methoxyphenoxyacetic acids (No. 6—9) in Table 3 as expected from their definitions. In this series of carboxylic acids, the A_{IV}/A_I, as well as $\Delta\nu$ values indicate that the intramolecular hydrogen bond becomes more favorable in the following order of 6-substituent: $H < Br < CH_3$. The bulky 6-substituent presumably favors the intramolecular hydrogen bond of this type by preventing the carboxylic acid to take the "*s-trans*" conformation[25] (**6**) which is unfavorable for the hydrogen bond formation.



"*s-cis*" conformation

(**5**)



"*s-trans*" conformation

(**6**)

Another weak absorption (band III in Table 3) may exist at about 3440 cm^{-1}. But the existence and the assignment is not certain and to be further investigated.

The authors are grateful to Prof. M. Ōki of the University of Tokyo and to Prof. H. Kakiuchi of Yokohama National University for their valuable advice. The authors also wish to express their hearty thanks to Prof. T. Shimanouchi and Prof. I. Nakagawa of the University of Tokyo for their useful suggestions and their kind permission to use infrared spectrophotometers.

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[18] The coplanarity is supported by comparing the ultraviolet spectra of the *o*-methoxyphenoxyacetic acid (λ_{max} 276.5 nm, ε_{max} 2790) with catechol dimethyl ether (λ_{max} 277 nm, ε_{max} 2920). Assuming the angle between the phenyl and the C–O–C planes (20°) as estimated from UV data and that the carboxyl O–H group lies 30° above the O=C–O plane in the *cis* conformation,[22] the conformation (**5**) of the hydrogen bonded species were plausible, from the Stewart's molecular models. In the assumed conformer the ArO and the carboxyl C=O grous take the most stable eclipsed conformation.[23]

[19] On the nomenclature of the carboxyl conformation, see Ref. 22.

[20] T. Miyazawa and K. S. Pitzer, *J. Chem. Phys.*, **30**, 1076 (1959).

[21] G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman & Co., San Francisco (1960), p. 82.

[22] C. P. Smyth, "Dielectric Behavior and Structure" McGraw Hill, New York (1954), p. 305.

[23] M. Hirota and T. Mizuno, Unpublished data.

[24] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York (1965), p. 19.

[25] The term "*s-trans*" and *s-cis*" refers to the conformations in which the methoxyl and carboxymethyl groups are the opposite and the same sides with respect to the C_{Ar}–O_{CH_2} bond, respectively. They are indifferent to the *cis* and *trans* conformations of carboxyl groups.