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Electronic Effects of the Substituents Containing the Thiocarbonyl Group

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The Hammett substituent constants, σ_m and σ_p , of 3-ethylthioureido, 3-ethylureido, thioacetamido, acetamido, methylaminothiocarbonyl, and methylaminocarbonyl groups were obtained from the dissociation constants of the *meta*- and *para*-substituted benzoic acids for the discussion of the electronic effects of the thiocarbonyl and carbonyl group. Their σ_I and σ_R values were also calculated from the σ_m and σ_p values. The result shows that the thiocarbonyl group attracts electrons from the adjacent nitrogen atom more strongly by resonance and more weakly by induction than the carbonyl group. As a whole, the thiocarbonyl group has stronger electron-withdrawing power than the carbonyl group.

It has been reported by Luttringhaus and Grohmann¹ that the dipole moments of *para,para'*-substituted thiobenzophenones are larger than those of the corresponding benzophenones when the *para,para'* substituents are strongly electron releasing by resonance and smaller when the substituents are not so strongly electron releasing by resonance. The fact may suggest that the thiocarbonyl group is more strongly electron withdrawing by resonance and more weakly so by induction than the carbonyl group. The concept that the thiocarbonyl group of thioamides has stronger resonance interaction with the adjacent nitrogen atom than the carbonyl group of amides is supported by the fact that thioamides have larger dipole moments,^{1,2} higher rotational energy barriers³ about the C-N bond, larger ¹³C-H coupling constants^{3e} in the nmr spectra of NCH₃, and shorter C-N bond distances^{2a} than the amides. The above concept about thioamides and amides is also discussed with respect to the infrared^{2a,d} and ultraviolet spectroscopy,^{2a,d,4} the ability to form hydrogen bonds,^{2e,5} and LCAO-MO treatment.^{3f,4,6} Further, the presumption that the electron density on the nitrogen of thioamides is lower than that of the corresponding amides may be derived from the pK_a value of thioacetamide,⁷ the coupling constants described above,^{3e} and Janssen's observation that the dissociation constants of the thiocarbonyl compounds of the acids AC(=X)BCH₂COOH (X = O and S, A = Me, B =

S; A = Me₂N, B = O; A = Me₂N, B = S) are larger than those of the carbonyl analogs.⁸

In the course of the study of 1-substituted aziridines and azetidines,⁹ it was found that there existed a remarkable difference between the reaction mechanism of the isomerization of the 1-acyl and 1-thioacyl compounds and that the thiocarbonyl compounds had the proton signals of the ring methylenes at lower magnetic field in the nmr spectra than the corresponding carbonyl compounds. For example, 1-thiobenzoylazetidine shows peaks of methylene protons at τ 5.70 and 7.73, while 1-benzoylazetidine shows these peaks at τ 5.86 and 7.76. These phenomena may be rationalized by the assumption that the thiocarbonyl group of thioamides and thioureas attracts electrons more strongly from the adjacent nitrogen than the carbonyl group of amides and ureas. Electronic effects of substituents containing the thiocarbonyl group have not been elucidated sufficiently, and no σ parameters of such substituents seem to have been reported except for those of thioureido group obtained from ¹⁹F nmr measurement ($\sigma_m = 0.22$, $\sigma_p = 0.16$, $\sigma_I = 0.29$, and $\sigma_R = -0.13$).¹⁰ In order to clarify the electronic effects of thioamide and thiourea linkage quantitatively and to compare them with those of amide and urea linkage, the Hammett σ constants were determined from the dissociation constants of *meta*- or *para*-substituted benzoic acids.

Results

The substituted benzoic acids were prepared and purified as described in the Experimental Section and their physical properties and analyses are given in Table I.

The Hammett σ values obtained from the dissociation

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TABLE I
 meta- or para-SUBSTITUTED BENZOIC ACIDS

Substituent	Registry no.	Mp, °C ^a	Formula	Calcd, %			Found, %			Ir spectra, ^b cm ⁻¹	
				C	H	N	C	H	N	ν_{NH}	$\nu_{\text{C=O}}$
m-CH ₃ CSNH	23667-97-2	224 dec	C ₉ H ₉ NO ₂ S	55.38	4.65	7.18	55.64	4.80	7.09	3160	1680
m-CH ₃ CONH	587-48-4	246-247 ^c	C ₉ H ₉ NO ₂	60.33	5.06	7.82	60.01	4.93	7.82	3360	1705, 1640
p-CH ₃ CSNH	23667-98-3	219 dec	C ₉ H ₉ NO ₂ S	55.38	4.65	7.18	55.75	4.85	7.12	3150	1690
p-CH ₃ CONH	556-08-1	256-257 ^d	C ₉ H ₉ NO ₂	60.33	5.06	7.82	59.98	5.04	7.82	3330	1675
m-C ₂ H ₅ NHCSNH	19384-17-9	204-206	C ₁₀ H ₁₂ N ₂ O ₂ S	53.57	5.39	12.50	53.79	5.17	12.52	3270, 3230	1685
m-C ₂ H ₅ NHCONH	23754-39-4	234 dec	C ₁₀ H ₁₂ N ₂ O ₂	57.68	5.81	13.46	57.44	5.84	13.45	3340, 3290	1690, 1640
p-C ₂ H ₅ NHCSNH	15863-32-8	208 dec	C ₁₀ H ₁₂ N ₂ O ₂ S	53.57	5.39	12.50	53.59	5.50	12.29	3300, 3250	1650
p-C ₂ H ₅ NHCONH	23754-41-8	>280	C ₁₀ H ₁₂ N ₂ O ₂	57.68	5.81	13.46	57.74	5.64	13.39	3320	1680, 1643
m-CH ₃ NHCS	23754-42-9	190-192	C ₉ H ₉ NO ₂ S	55.38	4.65	7.18	55.50	4.53	7.15	3340	1675
m-CH ₃ NHCO	23754-43-0	233-234	C ₉ H ₉ NO ₂	60.33	5.06	7.82	60.21	5.02	7.79	3300	1683, 1640
p-CH ₃ NHCS	23754-44-1	228-229	C ₉ H ₉ NO ₂ S	55.38	4.65	7.18	55.34	4.58	7.19	3340	1680
p-CH ₃ NHCO	23754-45-2	260-262	C ₉ H ₉ NO ₂	60.33	5.06	7.82	60.13	5.01	7.73	3300	1685 ^e

^a All melting points are uncorrected. ^b The infrared spectra were measured as a Nujol mull. ^c Literature mp 248°, 250°: B. Pawlewski, *Ber.*, **35**, 110 (1902); F. Ullman and J. B. Uzbachian, *ibid.*, **36**, 1797 (1903). ^d Literature mp 250-251°, 256.5°, 255°: F. Ullman and J. B. Uzbachian, *ibid.*, **36**, 1797 (1903); A. Kaaiser, *ibid.*, **18**, 2942 (1885); G. W. K. Cevill and J. M. Vincent, *J. Soc. Chem. Ind.*, **67**, 25 (1948). ^e Broad.

TABLE II

SUBSTITUENT CONSTANTS OBTAINED FROM THE DISSOCIATION CONSTANTS OF meta- or para-SUBSTITUTED BENZOIC ACIDS IN 50% AQUEOUS ETHANOL AT 25°

Substituent	σ_m	σ_p	σ_I	σ_R
CH ₃ CSNH	0.24	0.12	0.30	-0.18
CH ₃ CONH ^a	0.16 ^b	-0.07 ^c	0.27 ^d	-0.34 ^e
C ₂ H ₅ NHCSNH	0.30	0.07	0.41	-0.34
C ₂ H ₅ NHCONH	0.04	-0.26	0.19	-0.45
CH ₃ NHCS	0.30	0.34	0.28	0.06
CH ₃ NHCO	0.35	0.36	0.35	0.02

^a The σ values of the acetamido group reported in the literature were obtained from the dissociation constants or the reactivities [D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958); R. W. Taft, Jr., N. C. Deno, and P. S. Skell, *Ann. Rev. Phys. Chem.*, **9**, 287 (1958)] and from ¹⁹F nmr chemical shift measured in specific solvents [ref 10; R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *J. Amer. Chem. Soc.*, **85**, 709 (1963)]. ^b Literature (McDaniel and Brown) 0.15, 0.270; (ref 10) 0.13 (measured in acetonitrile). ^c Literature (McDaniel and Brown) -0.06, -0.015, -0.053; (ref 10) 0.02 (measured in acetonitrile). ^d Literature (Taft, Deno, *et al.*) 0.28; (ref 10) 0.24 (measured in acetonitrile); (Taft, Price, *et al.*) 0.20 (measured in dimethylformamide), 0.24 ± 0.01 (measured in protonic solvents which are no more acidic than formic acid). ^e Literature (Taft, Deno, *et al.*) -0.22; (ref 10) -0.22 (measured in acetonitrile).

tion constants are summarized in Table II. Taft and Lewis¹¹ have shown that σ values can be divided fairly well into inductive, σ_I , and resonance contribution, σ_R , by the following formulas: $\sigma_I = 1/2(3\sigma_m - \sigma_p)$; $\sigma_R = 3/2(\sigma_p - \sigma_m)$. The values of σ_I and σ_R thus obtained are also shown in Table II.

Discussion

Since such substituents as thioacetamido, acetamido, 3-ethylthioureido, and 3-ethylureido group are attached to other groups at the same element, nitrogen, the values of σ_I of these substituents may be considered as the indices of the electron density of the nitrogen atom. As shown in Table II, the σ_I value of the 3-ethylthioureido group is greater than that of the 3-ethylureido group and that of the thioacetamido group seems to be greater than that of the acetamido group. Therefore, it may be concluded that the thiocarbonyl

group of thioamide and thiourea linkage attracts electrons more strongly from the adjacent nitrogen atom than the carbonyl group of the amide and urea linkage does. The electronic effects of substituents may be regarded as the sum of inductive and resonance effects,¹¹ and in some cases the inductive effect is rationalized by electronegativity of particular atoms of substituents.¹² As the electronegativity of sulfur is smaller than that of oxygen,¹³ the thiocarbonyl group should have weaker electron-withdrawing power by induction than the carbonyl group, and this seems to be shown by the fact that the σ_I value of the methylaminothiocarbonyl group is smaller than that of the methylaminocarbonyl group. Accordingly, the stronger electron-withdrawing power of the thiocarbonyl group may be attributable to resonance rather than to induction. It is pointed out by many authors that in the resonance $-\text{C}(=\text{X})\text{N} < \leftrightarrow$
 $-\text{C}(\text{X}^-)=\text{N}^+ < (\text{X} = \text{O}, \text{S})$, the dipolar canonical form contributes more in thioamides and thioureas ($\text{X} = \text{S}$) than in amides and ureas ($\text{X} = \text{O}$). The phenomenon is considered to be closely related to the fact that heavy elements hardly form $p\pi-p\pi$ multiple bonds. The reason why bivalent sulfur has less tendency to form double bonds than oxygen has been speculated in the literature as follows. (A) the contraction of bond distance to form multiple bonds may be more difficult for sulfur, which has ten electrons in the inner shells, than for oxygen, which has only two.^{2a,d} The repulsion of inner-shell electrons in general bonding has been discussed from the viewpoint of the repulsion energy of nonbonding electrons.¹⁴ (B) Because the 2p orbital of oxygen is roughly as large as that of carbon, the two orbitals will overlap well.^{5a} However, as the 3p orbital of sulfur is considerably larger than the 2p orbital of oxygen, the 3p and the 2p orbital will not overlap so well.^{5a} (C) Since the 3p orbital has two nodes where the signs of the four lobes are reversed, the $2p\pi-3p\pi$ bonding will have partial antibonding charac-

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ter and lower overlap integral value than the $2p\pi-2p\pi$ bonding, as shown in Figure 1.¹⁵ Speculations B and C treat of the overlap of p orbitals, but the former seems to be unable to rationalize the fact that $p\pi-p\pi$ multiple bonds between heavy elements of the same size also are hardly formed, for example, the fact that the double bond between silicons is formed very difficultly.¹⁶ Therefore, C seems to be better than B.

The second-row elements have d orbitals available while the first-row elements have not, and Rakshys, *et al.*, have shown that the $2p\pi-3d\pi$ interaction between aromatic rings and tricoordinated phosphorus substituents is considerably important.^{12b} The stronger electron-attracting power of the thiocarbonyl group may be partly attributable to the ability of the 3d orbitals of sulfur to accept electrons from the 2p orbitals of carbon by the $2p\pi-3d\pi$ interaction.

Experimental Section¹⁷

***m*-Thioacetamidobenzoic Acid.**—To a solution of 3.0 g (0.02 mol) of thioacetylthioglycolic acid and 0.8 g of sodium hydroxide in 20 ml of water was added a solution of 2.7 g (0.02 mol) of *m*-aminobenzoic acid in 20 ml of water. The reaction mixture was left standing for 1 hr at room temperature and acidified with dilute hydrochloric acid. The resulted solid was separated by filtration, washed with cold water, and recrystallized from ethanol-water or ethanol only. The yield was ca. 80% after a recrystallization. *p*-Thioacetamidobenzoic acid was prepared in the same way from *p*-aminobenzoic acid and thioacetylthioglycolic acid. Thioacetylthioglycolic acid was obtained by the method of Jensen and Pedersen.¹⁸

***m*-Acetamidobenzoic Acid.**—To an equimolar mixture of *m*-aminobenzoic acid and triethylamine in tetrahydrofuran, an equimolar amount of acetyl chloride in tetrahydrofuran was added dropwise with stirring and cooling. After the solution had been stirred for 1 hr, the solvent was removed from the reaction mixture. The residue was washed with cold water, dried, and recrystallized from ethanol. *p*-Acetamidobenzoic acid was synthesized from acetyl chloride and *p*-aminobenzoic acid in the same manner.

***m*-(3-Ethylthioureido)benzoic Acid.**—Equimolar amounts of ethyl isothiocyanate and the sodium *m*-aminobenzoate were refluxed in methanol for 2 hr. After the methanol was removed from the reaction mixture, the residue was dissolved in water and acidified with cold, dilute hydrochloric acid. The resulting precipitate was collected on a filter and recrystallized from methanol. *p*-(3-Ethylthioureido)benzoic acid was prepared from ethyl isothiocyanate and *p*-aminobenzoic acid in a similar manner.

***m*-(3-Ethylureido)benzoic acid** was prepared from ethyl isocyanate and *m*-aminobenzoic acid in tetrahydrofuran and purified by repeated recrystallizations from ethanol. The *para* isomer was obtained in the same way from ethyl isocyanate and *p*-aminobenzoic acid.

***m*-Methylaminocarbonylbenzoic Acid Methyl Ester.**—Isophthalic acid monomethyl ester was prepared by the method of Wohl¹⁹ from dimethyl isophthalate. The monomethyl ester was heated under reflux with excess thionyl chloride until the gas evolution ceased to give isophthalic acid chloride monomethyl ester, bp 155° (22 mm). To an aqueous solution of 2.1 mol of monomethylamine was added a solution of isophthaloyl chloride monomethyl ester in dry tetrahydrofuran dropwise with stirring below 0°. Immediately after the addition was over, the tetrahydrofuran was removed from the mixture under reduced pressure without heating. The remained aqueous solution was acidified with hydrochloric acid and ice. The resultant solid was collected on a filter, washed with cold water, and dried. The infrared spectrum of the solid had absorptions at 3280 (NH), 1730, and 1645 cm^{-1} (two C=O).

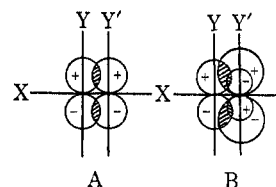


Figure 1.—(A) $2p\pi-2p\pi$ bonding; (B) $2p\pi-3p\pi$ bonding.

***p*-Methylaminocarbonylbenzoic Acid Methyl Ester.**—Terephthalic acid monomethyl ester was obtained by the method of Cohen.²⁰ The reaction between the ester and thionyl chloride was carried out in the same manner described above and the excess thionyl chloride was removed thoroughly under reduced pressure. The solid residue gave the title compound after the treatment with methylamine solution. The infrared spectrum had bands at 3360 (NH), 1740, and 1640 cm^{-1} (two C=O).

***m*-Methylaminothiocarbonylbenzoic Acid Methyl Ester.**—*m*-Methylaminocarbonylbenzoic acid methyl ester (3.0 g) and powdered phosphorus pentasulfide (1.0 g) were refluxed in 40 ml of xylene for 1 hr with stirring and the additional 60 ml of xylene was added to the reaction mixture. The hot solution was filtered to remove solid impurities and the xylene was removed from the filtrate under reduced pressure. The residue was recrystallized from *n*-hexane-benzene to give 3.0 g (70% yield) of yellow needles, mp 69–70°.

Anal. Calcd for $\text{C}_{10}\text{H}_{11}\text{NO}_2\text{S}$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.49; H, 5.41; N, 6.63.

The *para* isomer was prepared in a similar manner in 73% yield, melted at 141–141.5°, and had bands at 3350 (NH) and 1713 cm^{-1} (C=O) in its infrared spectrum.

Anal. Calcd for $\text{C}_{10}\text{H}_{11}\text{NOS}$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.68; H, 5.34; N, 6.57.

Hydrolysis of *meta*- or *para*-Substituted Benzoic Acid Methyl Esters.—Equimolar amounts of methylaminothiocarbonylbenzoic acid methyl esters or methylaminocarbonylbenzoic acid methyl esters and potassium hydroxide were heated in dry methanol under reflux for 1 hr and the methanol was removed. The residue was dissolved in water and filtered to remove solid impurities. The filtrate was acidified with hydrochloric acid and ice. The resultant solid was collected on a filter, dried, and recrystallized from ethanol-water or *n*-hexane-ethanol.

Determination of Dissociation Constants and ρ Value.—Because of the limited solubility of the benzoic acids in water, their dissociation constants were determined in 50% aqueous ethanol at 25° in the same way as reported by Monagle, Mengenhauser, and Jones.²¹ The ρ value for the dissociation of benzoic acids in this solvent system was determined. Treatment of the dissociation constants of *m*- and *p*-chlorobenzoic acid, benzoic acid, *p*-toluic acid, and *p*-anisic acid with the method of least squares gave 1.48 as the ρ value, 0.98 as the correlation coefficient γ , and 0.12 as the standard deviation. The ρ value was smaller than the reported values, 1.570,²² 1.681,²¹ and 1.851.²³

Registry No.—*m*-Methylaminocarbonylbenzoic acid methyl ester, 23668-00-0; *p*-methylaminocarbonylbenzoic acid methyl ester, 23754-46-3; *m*-methylaminothiocarbonylbenzoic acid methyl ester, 23754-47-4; *p*-methylaminothiocarbonylbenzoic acid methyl ester, 23754-48-5.

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