was obtained from the mother liquors of the (a) and (b) recrystallization.

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Evidence for the Expansion of the Valence Shell of Divalent Sulfur[1]

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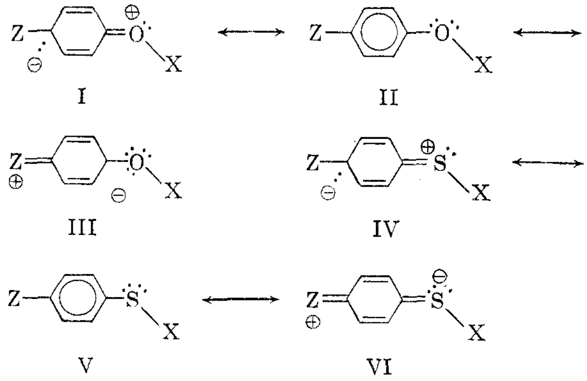
Received September 15, 1960

Because sulfur has unoccupied 3*d*-orbitals, it has the possibility of expanding its valence shell through electron-pair acceptor type conjugation. When sulfur is attached directly to a phenyl ring this electron-pair acceptor conjugation presumably occurs *via* overlap between a π-orbital on carbon and an unoccupied 3*d*-orbital on sulfur to form a $(p\text{-}d)\pi$ bond.

Bordwell and Boutan[2] concluded on the basis of pK_a data and a qualitative Hammett σ treatment that electron-pair acceptor type conjugation for divalent sulfur is usually small or negligible. Application of recent modifications of the Hammett σ treatment[3] which allow semiquantitative evaluation of resonance effects demonstrates that some revision of these conclusions is necessary.

Bordwell and Boutan reasoned that if sulfur expanded its valence shell the resonance form (VI) would be more important than form (III) and a $-$R *para-* substituent (Z) would be more electron donating by resonance in the ionization of a substituted thiophenol than in the ionization of the corresponding phenol, *i.e.*, the resonance effect of a $-$R *para-* substituent (Z) would have a larger negative value in the ionization of a thiophenol than in that of the corresponding phenol.[4]



I, II, III, IV, V, VI

They looked for this resonance effect, but their treatment of the data did not show it (*cf.* results listed in Table I) and it was therefore assumed to be absent. However, they arrived at their conclusions *via* the qualitative relationship:

$$\sigma_p - \sigma_m \cong para\text{-resonance effect}$$

which neglects small but significant resonance effects due to *meta-* substituents. Resonance values ($\bar{\sigma}_R$) calculated by the method of Taft and Lewis[3] (given in Table I), which considers resonance interactions from the *meta-* position, show that the effect is present, and although small, is outside of experimental error.

TABLE I

Comparison of ($\sigma_p - \sigma_m$) Values with $\bar{\sigma}_R$Values

Z	$\sigma_p - \sigma_m$ (ionization of phenols)	$\sigma_p - \sigma_m$ (ionization of thiophenols)	$\bar{\sigma}_R{}^a$ (ionization of phenols)	$\bar{\sigma}_R{}^a$ (ionization of thiophenols)
$-OCH_3$	-0.24	-0.21	-0.36	-0.48
$-N(CH_3)_2$	-0.16	-0.17	-0.21	-0.33

[a] These $\bar{\sigma}_R$ values were calculated using the ρ_I values given in Table II of reference (3) and the aliphatic σ_I values given by Taft and Lewis in Table I of reference (3) and Table II of *J. Am. Chem. Soc.*, **80**, 2436 (1958).

Participation by sulfur in electron-pair acceptor type conjugation should increase as the X-group attached to sulfur becomes more electron withdrawing by inductive and conjugative interaction (as measured *qualitatively* by the σ_p value of the X-group). This follows since such withdrawal would reduce the contribution of resonance form (IV) and also contract the 3*d*-orbitals making them less diffuse and therefore capable of greater overlap with a 2*p*-orbital on carbon. Table II shows that this effect is actually observed. The $\bar{\sigma}_R$ values for $-\overset{\cdot\cdot}{\text{S}}\diagdown_{\text{X}}$ qualitatively follow the σ_p values of X, increasing from negative numbers (net electron doner action by $-\overset{\cdot\cdot}{\text{S}}\diagdown_{\text{X}}$) when X is CH_3 to *positive* numbers (net electron acceptor action by $-\overset{\cdot\cdot}{\text{S}}\diagdown_{\text{X}}$) when X is $COCH_3$ and CN. In each case the $\bar{\sigma}_R$ values are *more positive* for the ionization of the substituted phenol than for that of the corresponding substituted benzoic acid, as would be expected

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[1] This work was supported in part by the Office of Naval Research, Project NR055-328.

[2] F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **78**, 854 (1956).

[3] R. W. Taft, Jr. and I. C. Lewis, *J. Am. Chem. Soc.*, **81**, 5343 (1959).

[4] As a result of resonance form (VI), valence shell expansion by sulfur would be expected to stabilize the substituted thiophenol relative to the corresponding thiophenylate ion because of the negative charge on sulfur in the anion. This effect should be very much smaller in the case of the substituted phenols; consequently, the ionization constant of thiophenol would be decreased more by the introduction of a $-$R *para* substituent (Z) than would the ionization constant of phenol.

if sulfur were participating in electron-pair acceptor type conjugation.

TABLE II

QUALITATIVE RELATIONSHIP BETWEEN $\bar{\sigma}_R$ VALUES FOR $-\overset{..}{S}\diagdown_X$ AND $\bar{\sigma}_R$ VALUES FOR X

$-\overset{..}{S}\diagdown_X$ Group	σ_p for X[a]	$\bar{\sigma}_R$ for $-\overset{..}{S}\diagdown_X$[b] (ionization of benzoic acids)	$\bar{\sigma}_R$ for $-\overset{..}{S}\diagdown_X$[b] (ionization of phenols)
$-SCH_3$	−0.17	−0.24	−0.03
$-SCOCH_3$	+0.52	+0.10	+0.12
—SCN	+0.63	+0.06	+0.14

[a] H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953). [b] The $\bar{\sigma}_R$ values for $-\overset{..}{S}\diagdown_X$ were calculated from the data of Bordwell and Boutan (2) using the ρ_I values given in Table II of reference (3). The aliphatic σ_I values of Taft and Lewis were used (see (*a*), Table I) except for the thiolacetoxy ($-SCOCH_3$) and thiocyanate groups. The σ_I value for the thiolacetoxy group was obtained from the data of Bordwell and Boutan[2] using equations (1) and (6) of reference (3) and the ρ_I and α values given in Table II of reference (3). The σ_I value of the thiocyanate group has not been experimentally determined, and was estimated from the equation:

$$\sigma_{I_{-AX}} = \sigma_{I_{-X}}\left(\frac{1}{2.8}\right) + \sigma_{I_{-AH}}$$

where 1/2.8 is a fall-off factor. This equation comes from unpublished work of R. W. Taft, Jr., and I. C. Lewis which is patterned after earlier work of G. E. K. Branch and M. Calvin, *The Theory of Organic Chemistry*, Prentice-Hall, Inc., New York, N. Y., 1941, pp. 201–225. In general, the method gives good agreement with experimental results.

Although the observed electron-pair acceptor participation by sulfur is small, the $(p\text{-}d)\pi$ conjugation need not necessarily be small since the observed effect could be the net result of $(p\text{-}d)\pi$ conjugation, such as shown in resonance form (VI), acting against a somewhat smaller magnitude of ordinary $(p\text{-}p)\pi$ conjugation of the type shown in resonance forms (IV) and (I).

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Phosphorus Pentoxide as a Reagent in Peptide Synthesis

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Received October 17, 1960

At the time Schramm and Wissman[1] reported on the use of phosphorus pentoxide for the synthesis of peptides, an essentially identical procedure was being developed in this laboratory. The purpose of this communication is, first of all, to report that, contrary to the findings of the above authors, racemization can occur when acylated peptides are employed as intermediates and, secondly, to supply additional information about the potential usefulness of this synthetic procedure.

The general procedure was as follows: A diethyl phosphite solution containing one mole of acylated amino acid, one mole of amino acid (or peptide) ester hydrochloride, and two moles of tri-*n*-butylamine, was added to a solution of phosphorus pentoxide in diethylphosphite. After being heated on a steam bath for forty minutes, the reaction mixture was poured into an aqueous sodium bicarbonate solution. Crystallization frequently occurred at this point. The reaction was carried out in a hood, since phosphine appeared as a by-product.

A number of the compounds not hitherto synthesized by this method are listed in Table I and include peptides containing the following amino acid residues: glycine, D-alanine, L-phenylalanine, L-tyrosine, L-tryptophan, ε-*N*-carbobenzoxy-L-lysine, and L-glutamic acid dibenzyl ester. The protecting groups include *N*-benzoyl, *N*-carbobenzoxy,

TABLE I

PEPTIDE DERIVATIVES

Compound[a]	Yield,[b] %	M.P., found	M.P., lit.
Z·Gly-Phe·OH(DL)	70[c]	160	160[d]
Z·Gly-Phe·OH(L)	64[c]	125–126	125–126[e]
Z·Ala-Gly·OBz(L)	85	112	111[f]
Z·Ala-Ala·OBz(D-D)	75	138	138[g]
Z·Phe-Gly·OC_2H_5(L)	77	109	109–110[h]
B·Gly-Z·Lys·OCH_3(L)[i]	75	145	145[j]
Tr·Gly-Gly·OC_2H_5	65	161	163[k]
Z·Ala-Tyr·OC_2H_5(L-L)	50	136	137[l]
Z·Try-Gly·OH(L)	32[c]	156	156[m]
Z·Gly-Try·OH(L)	50[c]	142	142[m]
Z·Ala-Glu·$(OBz)_2$(L-L)	65	103	104–105[n]

[a] The abbreviations are those of E. Brand and B. F. Erlanger, *J. Am. Chem. Soc.*, **73**, 3508 (1951). Tr = trityl = triphenylmethyl; B = benzoyl; Z = carbobenzoxy; Bz = benzyl. [b] Yield of purified products. [c] Over-all yield of coupling reaction and subsequent saponification of methyl ester. [d] J. Vaughan, Jr., and R. L. Osato, *J. Am. Chem. Soc.*, **74**, 676 (1952). [e] K. Hofmann and M. Bergmann, *J. Biol. Chem.*, **134**, 225 (1940) report $[\alpha]^{25}_{D}$ +38.5 (5.0% in ethanol); we find $[\alpha]^{25}_{D}$ +37.8 (0.5% in ethanol). [f] B. F. Erlanger and E. Brand, *J. Am. Chem. Soc.*, **73**, 3508 (1951). [g] This is m.p. of L-L isomer as reported in ref. *f*. [h] G. W. Anderson and R. W. Young, *J. Am. Chem. Soc.*, **74**, 5308 (1952). They also report $[\alpha]^{25}_{D}$ −16.0 (2% in ethanol); we find $[\alpha]^{25}_{D}$ −17.3 (2% in ethanol). [i] This compound was saponified and converted, by hydrogenolysis, to hippuryl L-lysine: $[\alpha]^{25}_{D}$ −5.2 (2.5% in water); ref. *e* reports the same rotation. [j] M. Bergmann, L. Zervas, and F. Ross, *J. Biol. Chem.*, **111**, 245 (1935). [k] G. Amiard, R. Heymes, and L. Velluz, *Bull. Soc. Chim. France*, 191 (1955). [l] M. Bergmann and J. S. Fruton, *J. Biol. Chem.*, **145**, 247 (1942). [m] E. L. Smith, *J. Biol. Chem.*, **175**, 39 (1948). [n] H. Sachs and E. Brand, *J. Am. Chem. Soc.*, **75**, 4608 (1953). They also report $[\alpha]^{25}_{D}$ −16.6 (2% in glacial acetic acid); we find $[\alpha]^{25}_{D}$ −16.8 (2% in glacial acetic acid).

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(1) G. Schramm and A. Wissman, *Ber.*, **91**, 1073 (1958).