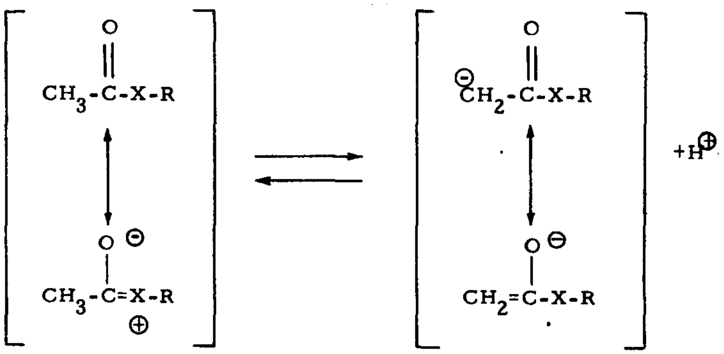
Tetrahedron Letters No.21, pp. 2007-2011, 1967. Pergamon Press Ltd. Printed in Great Britain.

ON THE ACIDITY OF THIOL ESTERS

G. Edwin Wilson, Jr.
Polytechnic Institute of Brooklyn
Brooklyn, New York 11201

(Received 5 October 1966; in revised form 27 March 1967)

Thiol esters, important in the biosynthesis of fatty acids, have been shown to be much more acidic than esters(1). In order to rationalize the large difference in acidities, Cronyn and co-workers(2) proposed that the ester anion would be greatly destabilized relative to an α-keto carbanion because of the competition between the ether oxygen atom and the carbanion to donate electrons to the carbonyl oxygen atom through the π-system. The thiol ester on the other hand would not be destabilized by a high degree of cross conjugation and would be intermediate between ketone and ester anions in stability. This would obtain because of the poor π-overlap of the 3p-orbital of sulfur with the 2p-orbital of oxygen and the consequent unimportance of the charge-separated resonance form to the thiol ester.



We were intrigued by the possibility that the relative acidities of the thiol ester and ester might be better explained as arising from the ability of the sulfur atom to accept electrons into the low-lying, vacant d orbitals(3, 4) even though classical resonance structures cannot be written to depict it. The relative magnitudes of the difference between the total energies of the neutral molecules and their respective anions as calculated by an extended Hückel Theory(5) should be indicative of the ease with which a proton would be lost. If the d orbitals are important as electron acceptors, the calculated energy difference for the thiol ester with d orbitals included should be smaller than the difference calculated when they are excluded. We chose to investigate methyl acetate and methyl thiolacetate as model systems. The bond angles and bond lengths of methyl acetate were those obtained by O'Gorman, Shand and Schomaker(6). The bond angles and bond lengths for the methyl thiolacetate were taken as those found for thiolacetic acid(7) and dimethyl sulfide (8) with a CSC angle of 100°. Our calculations on the ester and thiolester, using Slater orbitals and a value of K of 2.00 indicated a shallow energy minimum at the planar s-trans conformation, and we used that conformation throughout(9). The parameters (5, 10, 11) used are shown in Table I. For these calculations the carbanions were taken as flattened tetrahedra with a resultant carbon-hydrogen bond length of 0.96 A°. We found that, as expected, calculations using conformations involving tetrahedral carbanions led to energies higher than any for which the flattened tetrahedral carbanion model was used.

The conformation which served to minimize the energy placed the two hydrogen atoms in the plane of the carbon skeleton. For the data presented the carbon-carbon bond length of the anions was maintained the same as in the esters.

TABLE I

	Slater Exponents			Coulomb Integrals		
	s	p	d	s	p	d
Carbon	1.608	1.568		-21.40	-11.40	
Hydrogen	1.000			-13.60		
Oxygen	2.246	2.227		-35.57	-18.03	
Sulfur	2.122	1.827	2.050	-24.08	-17.32	-7.00

When only p orbitals are included in the calculations, the relative magnitudes of the total energy differences indicate that the acidities of ester and thiol ester should be practically identical, the ester being favored by 0.07 kcal. When the d orbitals of sulfur are included in the basis sets of both the thiolester and the anion, the ionization process for the thiol ester is calculated to be more favorable than that for the ester by 1.5 kcal (0.063 eV). The reliability of the calculated stabilization found when the d-orbitals are included in the basis set depends, of course, on the assumption that those inherently stabilizing factors always observed upon increasing the basis set will have a parallel and equivalent effect on the total energy of both the thiol ester and its anion. Additional assumptions are that solvation effects can be ignored and that the new attraction terms in the anions cancel when the energy differences are compared (5).

Evidence that our calculation supports the role of the d-orbital of the sulfur atom as electron acceptors is found by comparing the changes in bond orders (Table II) and atomic charges (Table III) in going from the neutral molecules to the carbanions. These changes, an increase in the carbon-sulfur bond order and an increase in the negative charge on the sulfur atom, arise mainly from population of molecular orbitals involving 2p-3d π-overlap.

It is interesting that the charge attenuation is about one-third of a unit per bond in the anions from both thiolester and ester. This is approximately that found for the decrease of the inductive effect of a polar substituent per added methylene unit (12, 13). In addition the charge decrease, especially at the ketonic oxygen atom, is much greater than would be expected on the basis of an allylic-type π-system. We find, however, that the sulfur atom of the thiolester anion bears about 7% of the charge as opposed to 3% for the ether oxygen atom of the ester anion. This is clearly incompatible with an inductive transfer on the basis of both electronegativities and bond lengths.

Shortening of the carbon-carbon bond length of the thiolester anion to 1.44 A$^{\circ}$ resulted in minimization of the energy. The carbonyl carbon atom now bears a larger fraction of the charge, but the attenuation in going to sulfur and oxygen remains approximately the same. Thus it appears that the unexpected charge distribution in our calculations cannot be attributed to the reduced π-overlap from an excessively long bond maintained between the carbons in the carbanions, but must indicate that the carbanionic center perturbs only the central atom and does not participate to any large degree in allylic type π-resonance.

Acknowledgement. The author thanks the computer center of the Polytechnic Institute of Brooklyn for the use of their facilities and Professor Almon G. Turner for use of his program.

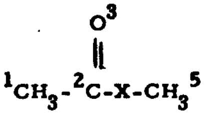
TABLE II

Total Energies and Bond Orders in Esters and Thiol Esters

	Ester		Thiol Ester				
	ester	anion	ester	ester[a]	anion	anion[a]	anion[b]
C-C	0.894	1.052	0.838	0.834	1.037	1.033	1.133
C-O	0.934	0.867	0.891	0.893	0.832	0.830	0.816
C-O, C-S	0.744	0.704	0.828	0.835	0.781	0.805	0.793
O-CH_3, S-CH_3	0.517	0.516	0.647	0.716	0.642	0.709	0.707
Total Energy (eV)	642.922	635.651	617.833	618.192	610.558	610.984	

TABLE III

Atomic Charges in Esters and Thiol Esters



$$\overset{O^3}{\overset{\|}{}}\quad {}^1CH_3\text{-}{}^2C\text{-}X\text{-}CH_3{}^5$$

	Ester		Thiol Ester				
	ester	anion	ester	ester[a]	anion	anion[a]	anion[b]
C_1	-0.391	-0.901	-0.366	-0.356	-0.867	-0.807	-0.744
C_2	1.475	1.217	1.258	1.254	1.002	0.983	0.954
C_3	-1.192	-1.242	-1.219	-1.212	-1.263	-1.260	-1.281
O_4, S_4	-0.809	-0.839	-0.374	-0.459	-0.415	-0.529	-0.549
C_5	0.145	0.145	-0.114	-0.081	-0.116	-0.083	-0.085

[a] with sulfur d orbitals included

[b] with sulfur d orbitals included and a C-C bond length of 1.44 A°

References and Footnotes

(1) L. Wessely and F. Lynen, *Federation Proc.*, **12**, 658 (1953);
C. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, **23**, 1147 (1940);
C. Schwarzenbach and E. Felder, *Helv. Chim. Acta*, **27**, 1701 (1944).

(2) M. W. Cronyn, M. P. Chang and R. A. Wall, *J. Am. Chem. Soc.*, **77**, 3031 (1955).

(3) The evidence for electron-accepting d-orbital stabilization of anions has been reviewed: D. J. Cram, *Fundamentals of Carbanion Chemistry*, Academic Press, N. Y. 1965, p. 71ff.

(4) Recent spectroscopic evidence for 2pπ-3dπ overlap in phenylsilanes and thioanisoles has been given by L. Goodman, A. Konstam, and L. H. Sommer, *J. Am. Chem. Soc.*, **87**, 1012 (1965) and L. Goodman and R. W. Taft, *J. Am. Chem. Soc.*, **87**, 4385 (1965).

(5) R. Hoffmann, *J. Chem. Phys.*, **39**, 1397 (1963); **40**, 2480 (1964); R. Hoffmann and W. N. Lipscomb, *J. Chem. Phys.*, **36**, 2179, 3489 (1962); **37**, 2872 (1962).

(6) J. M. O'Gorman, W. Shand, Jr., and V. Schomaker, *J. Am. Chem. Soc.*, **72**, 4222 (1950).

(7) W. Gordy, *J. Chem. Phys.*, **14**, 560 (1946).

(8) L. O. Brockway and H. O. Jenkins, *J. Am. Chem. Soc.*, **58**, 2036 (1936).

(9) The microwave spectrum(6) was interpreted to indicate an equilibrium dihedral angle of about 25°.

(10) E. Clementi and D. L. Raimondi, *J. Chem. Phys.*, **38**, 2686 (1963).

(11) T. Jordan, H. W. Smith, L. L. Lohr, Jr., and W. N. Lipscomb, *J. Am. Chem. Soc.*, **85**, 846 (1963).

(12) We wish to thank a referee for drawing our attention to this peculiar charge distribution.

(13) R. W. Taft, Jr., in M. S. Newman, *Steric Effects in Organic Chemistry*, Wiley, N. Y. 1956, p. 590ff.