$CHCl_3$) R_f 0.38; IR (CCl_4) 2778 (Bohlmann bands), 873 cm^{-1} (3-furyl); ^1H NMR δ 7.31 (m, 2 H, 3-furyl α-H), 6.36 (m, 1 , 3-furyl β-H), 3.60 (dd, J = 10.4 and 3.0 Hz, 1 H, C-2 H), 2.78 (q'd, 1 H, C-6 H), 1.05 (d, J , 6.6 Hz, 3 H, C-2 CH_3); ^{13}C NMR, see Table I; high-resolution MS, obsd/calcd mass (formula) 165.1151/165.1152 ($C_{10}H_{15}NO$).

Fraction E4 was chromatographed on a 1 × 11 cm column of neutral fractions and a 30-ml $CHCl_3$ fraction (F4). Fraction F4 was chromatographed on a 0.7 × 2-cm column of neutral Alumina (activity 2) with 150 mL of CH_2Cl_2 (G1) and two 75-mL portions of $CHCl_3$–CH_2Cl_2 (1:9) (G2 and G3). Fractions F3 (3 mg) and G3 (7 mg) were combined and consisted of pure **22**: GLC (column E, 150 °C) R_t 6.06; TLC (Alumina, twice developed, once with CH_2Cl_2 and then $CHCl_3$) R_f 0.31; IR (CCl_4) 2718 (very weak Bohlmann bands), 873 cm^{-1} (3-furyl); ^1H NMR δ 7.24–7.44 (m, 2 H, 3-furyl α-H), 6.36 (m, 1 H, 3-furyl β-H), 4.10 (t, J = 4 Hz, 1 H, C-2 H), 3.04 (q'd, J = 7.0 and 2.2 Hz, 1 H, C-6 H), 1.11 (d, J = 6.0 Hz, 3 H, C-6 CH_3); ^{13}C NMR, see Table I; high-resolution MS, obsd/calcd mass (formula) 165.1173/165.1152 ($C_{10}H_{15}NO$).

Registry No.—**1**, 61949-86-8; **2**, 61949-87-9; **3**, 110-93-0; **4**, 53067-23-5; **5**, 61900-43-4; **6**, 61900-44-5; **7**, 61900-45-6; **8**, 61900-46-7; **9**, 61900-47-8; **13**, 61900-48-9; **15**, 61586-90-1; **17**, 61900-30-9; **18**, 61900-31-0; **19**, 61900-32-1; **20**, 61900-33-2; **21**, 61900-34-3; **22**, 61900-35-4; **23**, 61900-36-5; **24**, 61900-37-6; **25**, 61900-38-7; **27**, 61949-85-7; dimethyl carbonate, 616-38-6; hydroxylamine HCl, 5470-11-1; dimethyl sulfate, 77-78-1; 3-furoyl chloride, 26214-65-3; 5-aminopentanoic acid, 660-88-8; 5-(3-furamido)hexanoate, 61900-39-8; (−)-nuphenine, 4850-01-5; (−)-anhydronupharamine, 4849-88-1.

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(17) All 3-furyl carbon resonance values, except that for the nonprotonated carbon in **27**, fall within the range of values for each of the four types of carbon atoms as found in: R. T. LaLonde, T. N. Donvito, and A. I-M. Tsai, *Can. J. Chem.*, **53**, 1714 (1975). The nonprotonated 3-furyl carbon in **27** falls at δ 128.6 ppm, which is 0.5 ppm below the lower limit of the range for this type of carbon. The resonance values for the vinylmethyl and olefinic carbons correspond to those given in: J. B. Stothers, ref 16, pp 72 and 82.
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(19) Our ^{13}C NMR resonance assignments for anhydronupharamine agree with those of another study [S. Yasuda, M. Hanaoka, and Y. Arata, *Chem. Pharm. Bull.*, **24**, 2521 (1976)] which we became aware of after this paper had been submitted for publication.

A Carbon-13 Nuclear Magnetic Resonance Study of Thiol Esters

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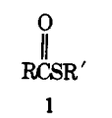
The ^{13}C NMR chemical shifts for each of the carbons of a number of simple thiol esters have been measured in Me_2SO-d_6 and $CDCl_3$ and the results related to known chemical properties of the thiol ester function. In general the chemical shift of the thiol ester carbonyl carbon occurs some 15–20 ppm further downfield than that found for all other carboxylic acid derivatives reported to date. The carbon α to the carbonyl function in thiol esters is also shifted downfield by about 10 ppm relative to the α carbon in acids, oxygen esters, or amides. The effect of carbon group and halogen substituents on thiol ester chemical shifts has been analyzed. A solvent study on β-hydroxy thiol esters shows that the carbonyl carbon is shielded in Me_2SO-d_6 relative to $CDCl_3$, which may be attributed to intramolecular hydrogen bonding in the latter solvent. Carbon-13 chemical shift changes resulting from conversion of mercaptans to thiol ester derivatives indicate relatively little difference between *S-tert*-butyl and other types of *S*-alkyl thiol esters in contrast to results obtained previously with *tert*-butyl oxygen esters.

The thiol ester group **1** is the ester function of choice in condensation and acyl transfer reactions occurring in biochemical systems.[1] In contrast to (oxygen) esters or amides, relatively little is known about the electronic structure of this group. As a result of our interest in the chemistry and properties of thiol esters, we have undertaken a ^{13}C NMR study of this class of compounds. A search of the literature has not produced any general ^{13}C NMR studies on the thiol ester function.[2] We have thus obtained natural abundance ^{13}C NMR spectra for some 30 different compounds. These results are discussed in connection with ^{13}C NMR data available for other carbonyl derivatives.[3,4] Substituent effects of the thiol ester group are analyzed and the effect of structure on thiol ester chemical shifts has been examined. Finally, we have focused attention on the relationship of these ^{13}C NMR results to the chemistry and biological properties of the thiol ester function.



1

Experimental Section

Spectra. The ^{13}C NMR spectra were obtained on ca. 20–25% (w/v) solutions in $DCCl_3$ or Me_2SO-d_6 using a Varian CFT-20 spectrometer

Table I. Carbon-13 Chemical Shifts for Thiol Ester Carbonyl Carbons[a]

O
‖
RCSR′

R	R′ Methyl	Ethyl	*n*-Propyl	Isopropyl	*n*-Butyl	*tert*-Butyl	Benzyl	Phenyl
Methyl	195.4	195.0	194.9	195.0	194.9[b]	195.6	194.5	193.2
		195.3	*195.6*	*195.7*	*195.2*	*196.3*	*194.7*	*193.3*
Ethyl		199.3		199.2		199.9		
						200.8		
Isopropyl						203.5	202.3	
						204.7		
Cyclopropyl						198.6		
Phenyl		191.2			191.0			
					191.7			
Chloromethyl						193.2	193.3	
1-Chloroethyl						196.6		
Dichloromethyl					191.2			
Acetyl								*(189.2)*[c,d]

[a] δ_C ppm from Me_4Si (internal standard) in Me_2SO-d_6. Numbers in italics refer to chemical shifts recorded in $CDCl_3$. [b] The reported value[2] in dioxane is 194.1 ppm. [c] The other carbonyl carbon in *S*-phenyl thiolpyruvate had a value of 193.2 ppm. [d] Registry no., 13884-99-6.

Table II. Carbon-13 Alkyl Carbon Chemical Shifts for Thiol Ester Derivatives[a]

O
‖
RCSR′

β α O α′ β′ γ′ δ′
C—C—C—S—C—C—C—C
‖
O

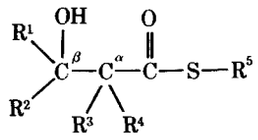
Registry no.	R	R′	α	β	α′	β′	γ′	δ′
1534-08-3	Methyl	Methyl	30.2		11.3			
625-60-5	Methyl	Ethyl	30.5[b]		23.1	14.7		
			30.5		*23.6*	*14.8*		
2307-10-0	Methyl	Propyl	30.5		30.5	22.7	13.1	
			30.6		*23.0*	*31.1*	*13.3*	
926-73-8	Methyl	Isopropyl	30.6[b]		34.4[b]	22.7		
			30.6		*34.8*	*23.0*		
928-47-2	Methyl	Butyl	30.5		28.3[c]	31.6	21.6	13.5
			30.5		*28.9*	*31.8*	*22.1*	*13.6*
999-90-6	Methyl	*tert*-Butyl	31.2		47.4	29.5		
			31.2		*47.8*	*29.8*		
32362-99-5	Methyl	Benzyl	30.1		32.7			
			30.2		*33.4*			
934-87-2	Methyl	Phenyl	30.1					
			30.0					
3232-39-1	Methyl	Acetyl	*32.6*					
2432-42-0	Ethyl	Ethyl	37.1	9.5	22.7	14.8		
2432-47-5	Ethyl	Isopropyl	37.0	9.4	34.1	22.8		
61540-13-4	Ethyl	*tert*-Butyl	37.3	9.2	47.1	29.4		
			37.9	*9.6*	*47.5*	*29.9*		
29786-94-5	Isopropyl	*tert*-Butyl	43.0[b]	19.2	46.9[b]	29.6		
			43.4	*19.4*	*47.3*	*29.9*		
61915-58-0	Isopropyl	Benzyl	42.4	19.1	32.2			
58058-56-3	Cyclopropyl	*tert*-Butyl	22.4	9.6	47.4	29.6		
1484-17-9	Phenyl	Ethyl			23.0	14.7		
7269-35-4	Phenyl	Butyl			28.3	31.4	21.7	13.5
					28.7	*31.8*	*22.1*	*13.6*
56377-45-8	Chloromethyl	*tert*-Butyl	48.1[b]		48.5[b]	29.3		
56377-58-3	Chloromethyl	Benzyl	48.1		33.0			
56377-47-0	1-Chloroethyl	*tert*-Butyl	59.7	21.5	48.8	29.5		
61915-59-1	Dichloromethyl	Butyl	70.1		(29.4)	(30.6)	21.3	13.4

[a] δ ppm from Me_4Si (internal standard) in Me_2SO-d_6. Chemical shifts recorded in italics refer to values obtained in $CDCl_3$. [b] Assignments based in part on off-resonance decoupled ^{13}C NMR spectra. [c] The reported values[2] in dioxane are 30.1 (α), 28.7 (α′), 32.1 (β′), 22.2 (γ′), and 13.6 (δ′).

with noise decoupling. The chemical shifts are referenced to internal Me_4Si. The precision of the chemical shift data is at least ±0.05 ppm (8K data points in the time domain for a 225 ppm spectral window).

Materials. *S*-Phenyl thiolacetate, γ-thiobutyrolactone, *S*-ethyl thiolpropionate, and diacetyl sulfide were obtained from Aldrich Chemical Co. *S*-Methyl thiolacetate, *S*-isopropyl thiolacetate, *S*-isopropyl thiolpropionate, and *S*-ethyl thiolbenzoate were purchased from Wateree Chemical Co. *S*-Propyl thiolacetate and *S*-butyl thiolacetate were obtained from Columbia and *S*-ethyl thiolacetate and *S*-butyl thiolbenzoate were purchased from Pfaltz and Bauer. The purity of these commercial samples was checked by ^1H NMR. They

Table III. Carbon-13 Chemical Shifts for Certain β-Hydroxy Thiol Esters in Me_2SO-d_6 and $CDCl_3$[a]



	β-Hydroxy thiol ester											Δδ Me_2SO-d_6 relative to $CDCl_3$					
Registry no.	R^1	R^2	R^3	R^4	R^5	Solvent	C=O	α	β	R^5		R^1	C=O	α	β	R^5		R^1
58058-57-4	Ph	Ph	H	H	$C(CH_3)_3$	Me_2SO-d_6	197.4	54.7	76.3	47.4[b]	29.3[c]	146.9[d]	−4.0	+0.6	−1.7	−1.5	−0.3	+1.0
						$CDCl_3$	*201.4*	*54.1*	*78.0*	*48.9*	*29.6*	*145.9*						
58058-60-9	Ph	Ph	H	H	CH_2Ph	Me_2SO-d_6	195.5	54.5	76.7	32.2[e]		147.0[d]	−4.0	+0.5	−1.2	−0.9		+1.4
						$CDCl_3$	*199.5*	*54.0*	*77.9*	*33.1*		*145.6*						
58058-61-0	Ph	Ph	H	H	Ph	Me_2SO-d_6	193.6	54.5	76.2			146.9[d]	−5.0	+0.6	−1.7			+1.3
						$CDCl_3$	*198.6*	*53.9*	*77.9*			*145.6*						
58105-75-2	Ph	H	CH_3[f]	CH_3[f]	$C(CH_3)_3$	Me_2SO-d_6	205.4	55.2	76.8	46.6[b]	29.5[c]	141.8[d]	−3.1	+0.3	−2.2	−1.0	0.0	+1.6
						$CDCl_3$	*208.5*	*54.9*	*79.0*	*47.6*	*29.5*	*140.2*						
41823-07-8	H	H	H	PH	Ph	Me_2SO-d_6	196.5	62.3[g]	63.4[g]				−1.8	+0.1	−1.1			
						$CDCl_3$	*198.3*	*62.2*	*64.5*									
42479-96-9	Ph	H	H	H	Ph	Me_2SO-d_6	194.2	52.9	69.6			144.2[d]	−2.5	+0.7	−1.1			+1.8
						$CDCl_3$	*196.7*	*52.2*	*70.7*			*142.4*						

[a] δ ppm from Me_4Si (internal standard) in Me_2SO-d_6. Numbers in italics refer to values obtained in $CDCl_3$. [b] Tertiary carbon of *tert*-butyl group. [c] Methyl of *tert*-butyl group. [d] Carbon one of the β-phenyl group. [e] Benzyl carbon. [f] The two α-methyl groups had chemical shifts of δ 20.0 and 21.5 in Me_2SO-d_6 and δ 19.5 and 23.5 in $CDCl_3$. [g] Assignments based in part on off-resonance decoupled spectra.

were all used without further purification. *S-tert*-Butyl thiolacetate,[5] *S*-benzyl thiolacetate,[6] *S-tert*-butyl thiolisobutyrate,[7] *S-tert*-butyl chlorothiolacetate,[8] *S*-phenyl thiolpyruvate,[9] *S-tert*-butyl cyclopropanecarbothioate,[10] *S-tert*-butyl α-chlorothiolpropionate,[11] *S*-benzyl chlorothiolacetate,[11] *S-tert*-butyl thiolpropionate,[12] α-methyl-γ-thiobutyrolactone,[12] *S-tert*-butyl β,β-diphenyl-β-hydroxythiolpropionate,[10] *S*-phenyl β,β-diphenyl-β-hydroxythiolpropionate,[10] *S-tert*-butyl α,α-dimethyl-β-phenyl-β-hydroxythiolpropionate,[10] *S*-phenyl β-phenyl-β-hydroxythiolpropionate,[10] and *S*-phenyl α-phenyl-β-hydroxythiolpropionate[13] were prepared according to literature methods.

S-Benzyl thioisobutyrate was obtained from isobutyryl chloride, benzyl mercaptan, and pyridine according to the procedure described previously for the synthesis of *S-tert*-butyl bromothiolacetate.[11] The *S*-benzyl thioisobutyrate was isolated as a colorless oil following distillation under reduced pressure: bp 150–152 °C (15 mm); $n^{23}D$ 1.5405; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.18 (d, 6 H, J = 7 Hz), 2.74 (septet, 1 H, J = 7 Hz) 4.13 (s, 2 H), 7.33 (s, 5 H); IR (film) 1680 cm^{-1}. Anal. Calcd for $C_{11}H_{14}OS$: C, 68.00; H, 7.26; S, 16.50. Found: C, 68.31; H, 7.25; S, 16.27.

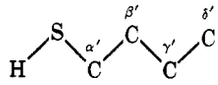
S-Butyl dichlorothiolacetate was obtained in a similar way[11] from dichloroacetyl chloride, butyl mercaptan, and pyridine as a colorless oil: $n^{28}D$ 1.4975; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.75–1.15 (t, 3 H), 1.15–2.0 (m, 4 H), 3.03 (t, 2 H), 6.17 (s, 1 H); IR (film) 1675 cm^{-1}. Anal. Calcd for $C_6H_{10}OSCl_2$: C, 35.83; H, 5.01; S, 15.94. Found: C, 35.66; H, 5.13; S, 16.12.

Results and Discussion

The chemical shifts (δ_c, ppm from Me_4Si) for a series of simple thiol esters are recorded in Tables I–III. The signals corresponding to the carbonyl carbons as well as many of the carbons attached to halogen or oxygen heteroatoms are easily distinguished as a result of their low field chemical shifts. For other carbons, assignments were based on readily recognizable trends for a particular type of carbon observed within a series of similar structures. For example, eight different *S-tert*-butyl thiol esters were examined. In all of these spectra taken in Me_2SO-d_6 we observed a high intensity peak between δ 29.2 and 29.7 which was assigned to the methyl groups, and a low intensity peak between δ 46.6 and 48.5 which was assigned to the tertiary carbon of the *tert*-butyl group. Certain assignments were more difficult and are based solely on analogy with the corresponding carbon in the parent alkanes, alcohols, ethers, mercaptans, and/or oxygen esters reported previously.[3,4] In many cases it was possible to confirm these assignments by single frequency off-resonance decoupling experiments. Where uncertainty still exists with respect to a given assignment, the number is indicated in brackets in Tables I–V. However, possible ambiguities in these assignments are not of major significance for the conclusions that we have drawn in our discussion.

Of considerable interest is the result that the chemical shift of the carbonyl carbon in thiol esters generally occurs in the 193–203-ppm range for aliphatic thiol esters. This value is some 15–20 ppm further downfield than that found for the carbonyl carbon of all other carboxylic acid derivatives reported to date[3,4] including the parent acids,[14,15] esters,[14,16] amides,[4,14,17] acid chlorides,[4,14,18] anhydrides,[4,14a] carboxylate salts,[15b] and other derivatives.[4] γ-Thiobutyrolactone and α-methyl-γ-thiobutyrolactone have carbonyl chemical shifts of 209.4 and 210.5 ppm, respectively, compared to a value of 178.0 ppm for γ-butyrolactone.[14] This marked difference in chemical shift, characteristic of the thiol ester carbonyl carbon, may potentially be exploited in numerous ways including the use of the ^{13}C NMR method in biochemical studies on coenzyme A thiol ester derivatives insofar as the thiol ester carbonyl carbon should appear further downfield than any other carbon in the complex coenzyme A structure. Our results would suggest a value of 193–195 ppm for the thiol ester carbonyl of acetyl CoA.[19] The 193–203-ppm range found for thiol esters closely approaches that reported for aldehydes and

Table IV. Carbon-13 Chemical Shifts for Simple Mercaptans[a]



Registry no.	Mercaptan	α′	β′	γ′	δ′
107-03-9	Propyl mercaptan[b]	(26.0)	(26.8)	12.8	
75-33-2	Isopropyl mercaptan	29.9[d]	27.4[d]		
109-79-5	Butyl mercaptan[c]	23.6	35.6	21.0	13.4
		24.3	*36.2*	*21.5*	*13.5*
75-66-1	*tert*-Butyl mercaptan	40.7	34.7		
		41.1	*35.0*		
100-53-8	Benzyl mercaptan	27.8			

[a] δ_C ppm from Me_4Si (internal standard) in Me_2SO-d_6. Chemical shifts recorded in italics are values obtained in $CDCl_3$. [b] The reported[38] values in CD_3OD are 26.4 (α′), 27.6 (β′), and 12.6 (γ′). [c] The reported[38] values in CD_3OD are 24.6 (α′), 37.1 (β′), 22.3 (γ′), and 13.9 (δ′). [d] Assignments based in part on off-resonance decoupled ^{13}C NMR spectra.

Table V. Carbon-13 Chemical Shift Changes (Δδ, ppm) Associated with Formation of Thiol Ester Derivatives of Mercaptans[a]

Thiol ester	α′	β′	γ′	δ′
S-Propyl thiolacetate	(+4.5)	(−4.1)	+0.3	
S-Isopropyl thiolacetate	+4.4	−4.7		
S-Butyl thiolacetate	+4.8	−4.1	+0.6	+0.1
	+4.6	*−4.4*	*+0.5*	*+0.1*
S-*tert*-Butyl thiolacetate	+6.7	−5.2		
	+6.7	*−5.2*		
S-Benzyl thiolacetate	+4.9			
S-Isopropyl thiolpropionate	+4.2	−4.6		
S-*tert*-Butyl thiolpropionate	+6.4	−5.3		
	+6.5	*−5.1*		
S-*tert*-Butyl thiolisobutyrate	+6.2	−5.1		
	+6.3	*−5.1*		
S-Benzyl thiolisobutyrate	+4.3			
S-*tert*-Butyl cyclopropanecarbothioate	+6.7	−5.1		
S-*tert*-Butyl chlorothiolacetate	+7.8	−5.3		
S-Benzyl chlorothiolacetate	+5.1			
S-*tert*-Butyl α-chlorothiolpropionate	+7.5	−5.2		
S-Butyl thiolbenzoate	+4.7	−4.2	+0.6	+0.1
	+4.4	*−4.5*	*+0.6*	*+0.1*

[a] The data represent chemical shifts of the *S*-alkyl carbons of the indicated thiol ester relative to the analogous carbon in the corresponding mercaptans. Comparisons were made in Me_2SO-d_6 or $CDCl_3$ (italics). The values were calculated from data in Tables II and IV.

ketones.[3,4] In this connection it is noteworthy that in many ways thiol esters resemble ketones or aldehydes in their chemical properties. For example, unlike oxygen esters, acids, or amides, thiol esters are rapidly reduced by sodium borohydride.[20] We have also recently found that the migratory aptitude of the thiol ester group is comparable to the ketone in the boron trifluoride induced rearrangement of α,β-epoxy carbonyl systems. Both groups migrate more readily than the oxygen ester.[21]

Many of the substituent effects observed earlier in ^{13}C NMR studies of other carbonyl compounds were also found in our analysis of thiol esters. For example, as in the case of aldehydes, ketones, acids, esters, and amides,[3,4] replacement of an α hydrogen with a methyl group causes a substantial downfield shift for the thiol ester carbonyl carbon (cf. Table I and the values for *S*-*tert*-butyl thiolacetate, thiolpropionate, and thiolisobutyrate). It is interesting that in the case of thiol esters the shift (~4 ppm) is somewhat greater than noted earlier (2–3 ppm) for aldehydes, ketones, acids, and oxygen esters.[3] A relatively large increment (4.5 ppm) is found, however, in comparing acetamide with propionamide.[4b] Substitution at the α position with chlorine causes an upfield change (1–2 ppm) in the chemical shift of the carbonyl carbon in Me_2SO-d_6 (cf. *S*-*tert*-butyl thiolacetate and chlorothiolacetate). A similar effect due to α-chlorine substitution has been observed for ketones, carboxylic acids, and acid chlorides.[3,4] Attachment of a phenyl group or a cyclopropane ring to the thiol ester carbonyl carbon also causes a substantial upfield shift (cf. Table I. Compare *S*-butyl thiolbenzoate with *S*-butyl thiolacetate and *S*-*tert*-butyl cyclopropanecarbothioate with *S*-*tert*-butyl thiolisobutyrate). In contrast to the marked changes in the carbonyl chemical shift caused by modification of the acyl portion of the thiol ester, relatively little change occurs when the hydrocarbon group attached to sulfur is modified. Thus, the carbonyl resonance for *S*-methyl, *S*-ethyl, *S*-propyl, *S*-isopropyl, *S*-butyl, and *S*-*tert*-butyl thiolacetates all come between 194.4 and 195.6 ppm in Me_2SO-d_6. An upfield shift of approximately 2 ppm occurs in *S*-phenyl thiolacetate (193.2 ppm in Me_2SO-d_6) and the carbonyl carbon of diacetyl sulfide [$(CH_3CO)_2S$] comes at still higher field (191.8 ppm in $CDCl_3$). A chemical shift of 194.5 ppm found for thioacetic acid has been ascribed to the thiocarbonyl group in tautomer **2**.[4] However, the weight of experimental evidence argues against a thiocarbonyl group in thioacetic acid favoring instead a carbonyl group as in tautomer **3**.[1c,22] The 194.5-ppm value obtained for thioacetic acid is in good agreement with structure **3** in view of the result that

2 **3**

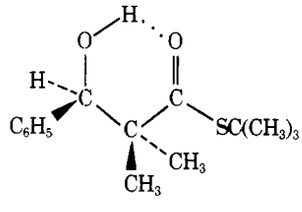
S-alkyl and *S*-aryl thiolacetates all fall in the 193–196-ppm range.

A semiempirical approach has been developed to relate carbonyl chemical shifts to the π bond polarity of the carbonyl function.[23] This π bond polarity depends to a considerable extent on the relative electron-withdrawing ability of attached groups as gauged by Taft's inductive parameter σ_I.[24] Based on this analysis the lower electron-attracting ability of sulfur compared to oxygen would result in greater shielding of the carbonyl carbon in oxygen esters relative to the corresponding thiol esters.[14,16] The effect of p–p π bonding in thiol esters on the chemical shift of the carbonyl carbon is less certain. Indeed the relative degree of resonance in thiol esters has recently been questioned by Noe[25] in a DNMR study of rotational barriers in thioacetic acid. This work suggests that there is considerably more resonance in thio acids than in the corresponding oxygen acids or esters in contradiction to conclusions reached in earlier studies.[1c,26,27]

The deshielding effect of the thiol ester function at the α carbon is very similar to that caused by a ketone or aldehyde group. Thus, the methyl carbon in *S*-alkyl and *S*-aryl thiolacetates occurs in the 30–31-ppm range (Table II) while the methyl carbon in acetaldehyde comes at 31 ppm and in aliphatic methyl ketones between 28 and 30 ppm.[3] In contrast, the methyl carbon in acetate esters[3,16f] or acetamides[17b] occurs at about 21 ppm.[3,16f] In this connection it is interesting to note

that the acidity of the α protons in thiol esters is comparable to that in ketones while both ketones and thiol esters are substantially more acidic than the corresponding oxygen esters.[28] Further, we have found recently that the nucleophilicity of thiol ester lithium enolates in substitution reactions with alkyl halides is considerably less than that of the corresponding oxygen ester lithium enolates.[12] Thus again in this instance we see a useful correlation of the ^{13}C NMR data with the chemical properties of thiol esters as compared to data available for ketones, esters, and amides.

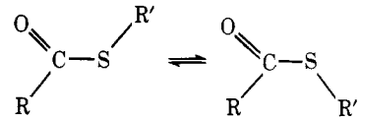
For simple thiol esters such as *S*-ethyl, *S*-phenyl, or *S*-butyl thiolacetates there is relatively little effect on chemical shift values as a result of a change in solvent from the very polar Me_2SO to the less polar chloroform. Generally we observed a slight downfield shift of between 0.1 and 0.6 ppm on going from Me_2SO-d_6 to $CDCl_3$ for the carbonyl carbon as well as most of the other carbons. This is consistent with earlier observations on the small effect of a change in solvent on the carbonyl chemical shift of acetone.[29] In contrast in a study of several β-hydroxy thiol esters we observed a marked downfield shift of the carbonyl carbon of between 1.8 and 5.0 ppm on going from Me_2SO-d_6 to $CDCl_3$ (Table III). It is likely that intramolecular hydrogen bonding is responsible for this solvent effect. Intramolecular hydrogen bonding would be relatively important in chloroform but less so in Me_2SO, where intermolecular hydrogen bonding with solvent molecules is expected to be more significant. Me_2SO has recently been used to rupture intramolecular hydrogen bonds in ^{13}C NMR studies of β-hydroxy (oxygen) esters and amides.[30,31] Hydrogen bonding interactions with ketone and ester carbonyl functions is reported to result in a downfield shift of the carbonyl carbon atom.[14a,29,32] Additional support for strong intramolecular hydrogen bonding in β-hydroxy thiol esters in $CDCl_3$ is seen in the relatively large chemical shift difference of the two α-methyl carbons in *S-tert*-butyl α,α-dimethyl-β-phenyl-β-hydroxythiolpropionate (**4**). The methyls occur at δ 20.0 and 21.5 in Me_2SO-d_6. One is shifted upfield (δ 19.5) and the other downfield (δ 23.5) in $CDCl_3$. Intramolecular hydrogen bonding in $CDCl_3$ would result in restricted rotation about the C_α–C_β and $C_{C=O}$–C_α bonds in **4** such that one methyl would be placed in close proximity to the phenyl group.



4

Also of interest is the result that the α carbon in the β-hydroxy thiol ester system is shielded (0.1–0.7 ppm) while the β carbon is deshielded (1.1–2.2 ppm) as a result of intramolecular hydrogen bonding in $CDCl_3$. This phenomenon was also seen in our analysis of 4-hydroxy-4-methylpentan-2-one [$CH_3COCH_2C(OH)(CH_3)_2$], which gave chemical shifts of 208.3 and 210.5 ppm for carbon 2, 55.8 and 54.2 ppm for carbon 3, and 68.6 and 69.6 ppm for carbon 4 in Me_2SO-d_6 and $CDCl_3$, respectively. Shielding of the α position is then due to increased importance of a fixed conformational state that is characteristic of the intramolecularly hydrogen bonded structure in $CDCl_3$ as opposed to the greater variety of conformations available to the β-hydroxy thiol ester in Me_2SO-d_6.

We have obtained ^{13}C NMR spectra of several simple mercaptans (Table IV) and with this information calculated α' and $\beta'\Delta\delta$ values for certain thiol ester derivatives (Table V). The $\beta'\Delta\delta$ values (C-2 esterification effect) found for thiol esters are in the same direction although somewhat larger than those found for oxygen esters.[16f,h] The fact that relatively little variation is seen in the $\beta'\Delta\delta$ values (5.2 ± 0.2 in Me_2SO-d_6) for a large number of *S-tert*-butyl esters would indicate that the C-2 esterification effect results primarily from interaction of the *S-tert*-butyl group with the carbonyl function rather than the R substituent in the acyl group. A similar pattern is seen for other types of *S*-alkyl thiol esters studied (Table V). This would support the conclusion that *Z* conformation **5** is the major conformation present in these thiol esters.



Z **5** *E* **6**

The origin of nonequivalence in the chemical shifts of syn and anti methyl groups in *N,N*-dimethylformamide has been attributed to electric field effects[33] as well as steric perturbations.[17a,34] An electric field argument has been suggested to account for the large $\alpha'\Delta\delta$ value (C-1 esterification effect) found for *tert*-butyl formate compared to a smaller value obtained for other formate esters.[16f] More recently chemical shifts have been evaluated for a large number of methyl, ethyl, isopropyl, and *tert*-butyl oxygen esters.[16h] A linear relationship was shown to exist between the ^{13}C chemical shifts of the α' carbon and the pK_a values of acids from which the esters were derived. This was explained as a consequence of the polar character of the $-C_{\alpha'}{}^{\delta+}-O_2{}^{\delta-}CR$ bond. With respect to variation of the *O*-alkyl group from primary to secondary and tertiary, the C-1 esterification effect ($\alpha'\Delta\delta$ values) can be correlated with increasing stability of the partial positive charge at the α' carbon.[16h] These results[16h] suggest that the electric field argument is not a major factor in determining this C-1 esterification effect. The results obtained with oxygen esters[16f,h] do not appear to be inconsistent with steric perturbation providing some contribution to the large $\alpha'\Delta\delta$ values found for *tert*-butyl oxygen esters. Steric perturbation resulting in greater deviation from coplanarity[35,36] for the ester function has recently been proposed to account for the large bathochromic shift in the ultraviolet found for *tert*-butyl acetate compared to other alkyl acetates.[37]

The $\alpha'\Delta\delta$ values for thiol esters (Table V) increase with increasing acidity of the acid from which the ester is derived in agreement with the conclusions of Pelletier.[16h] The C-1 esterification effect found for propyl, butyl, or isopropyl thiol esters is in the same direction and generally larger than that found for propyl, butyl, and isopropyl oxygen esters; however, the $\alpha'\Delta\delta$ value found for *S-tert*-butyl thiol esters is considerably smaller than that found for *tert*-butyl oxygen esters. The relatively small difference (~2 ppm) in $\alpha'\Delta\delta$ values between *S-tert*-butyl thiol esters and other types of *S*-alkyl thiol esters is of particular interest and should be contrasted with the very large difference (~10 ppm) found earlier for oxygen esters.[16f,h] In the thiol ester system we may expect some increase in the degree of polarization of the S–$C_{\alpha'}$ bond when comparing *S-tert*-butyl esters with other alkyl thiol esters, although this effect is expected to be smaller than in oxygen esters[16h] owing to the lower electronegativity of sulfur compared to oxygen. It would seem that this X–$C_{\alpha'}$ polarization explanation[16h] is sufficient to account for the variation in $\alpha'\delta$ values found for thiol esters without invoking steric perturbation in the *S-tert*-butyl thiol ester system. The larger size of sulfur compared to oxygen would leave the *tert*-butyl further removed from the acyl group in *S-tert*-butyl thiol esters relative to *tert*-butyl oxygen esters. The likelihood of steric perturbation is greater in the *tert*-butyl oxygen ester system.

To what extent this influences the $\alpha'\Delta\delta$ values in *tert*-butyl oxygen esters is not clear based on available information.

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Registry No.—Isobutyryl chloride, 79-30-1; dichloroacetyl chloride, 79-36-7.

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Phase-Transfer Catalyzed Syntheses. 5-Thiacyclohexenecarboxaldehydes and 3,4-Epoxy-2,5-dihydrothiophenes[1]

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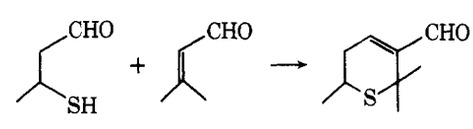
The phase-transfer catalyzed condensation of 3-thioacetoxyaldehydes with acrolein and crotonaldehyde leads to cyclized products **5–9**. Product distributions indicate that no equilibration of intermediates occurs as has been previously noted in pyridine solution. Condensations of α-mercaptocarbonyl compounds with 2-chloroacrylonitrile led to epoxides **11–14** in excellent yields. This reaction may be of some importance in biotin synthesis.

Recently, we have shown that the reaction of 3-mercaptoaldehydes (**1**) with conjugated carbonyl compounds affords, by a conjugate addition–aldol condensation sequence, an excellent route to substituted 5-thiacyclohexene-1-carboxaldehydes (**2**).[3] Compounds related to **2** have previously been shown[4] to be excellent synthons for stereospecific alkene synthesis. However, two drawbacks to the synthesis, as reported,[3] are evident. The first is the difficulty encountered in the purification of mercaptans **1**. Whereas the isomeric 2-mercaptoaldehydes exist largely as dimeric 2,5-dihydroxy-1,4-dithianes[5] which can be purified relatively easily, **1** are polymeric hemithioacetals which are uniformly evil-smelling, viscous oils that decompose (presumbly by dehydration) when distillation is attempted. This leads to complicated mixtures when the preparation of **2** is attempted. Although many examples of **1** are obtained pure enough for direct use in the cyclization, others are not and it was felt that an alternate preparation which avoided this difficulty would be desirable. Replacement of the thiol proton with a suitable protecting group which could be converted into the anion of **1** in situ would achieve this end. Furthermore, as the malodorous properties of most thiols are associated with the SH



1 **2**