

Preparation and Absorption Spectra of *p*-Mercaptocinnamic and *p*-Mercaptobenzoic Acids and Derivatives¹

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The properties of pure *trans-p*-mercaptocinnamic acid are correctly described and are different from compounds previously reported to have this structure. Acetylation of either the mercapto acid or its disulfide under alkaline conditions yields the same product. Air oxidation readily converts the thiol to the disulfide even in crystallizing solvents. The pK_a of the thiol group in both *p*-mercaptocinnamic and *p*-mercaptobenzoic acid is unexpectedly low, near that of the carboxyl group. Several esters and sulfides of *p*-mercaptocinnamic acid and *p*-mercaptobenzoic acid were prepared, and their ultraviolet spectra in neutral and alkaline solution were determined.

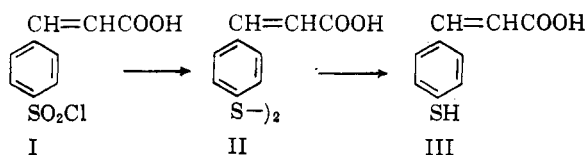
Recent work in this laboratory³ has led to investigations of the ultraviolet absorption spectra of cinnamic acid derivatives substituted with various sulfur-containing groups in the α - and β -positions. The applicability of these data to similar systems is limited because of the "crossed-conjugation" between the sulfur-containing groups and the cinnamic acid moiety. Therefore, it was desired to obtain a series of cinnamic and benzoic acids substituted with various sulfur-containing groups in the *para* positions. Included among these derivatives were the thiols, disulfides, and alkyl thioethers along with the respective methyl esters.

By means of the ultraviolet spectra of these compounds, one should obtain a quantitative picture of the effect of these groups on the cinnamic and benzoic acid chromophores, since these molecules exhibit continuous conjugated systems. It is also possible to obtain spectral changes by selectively ionizing either the thiol or carboxylic function by blocking the other, or by ionizing both acid groups, when these are present. This type of information can be helpful in the interpretation of the structure of analogous systems.

A survey of the literature indicates that there have been two reports on the preparation and properties of *p*-mercaptocinnamic acid. In 1952 Kurihara and Niwa⁴ published the synthesis of this compound by the reaction of sodium hydrosulfide on the diazonium salt of 4-aminocinnamic acid. The thiol was reported to crystallize in yellow needles and to melt at 95–96°. Later, in 1959, Overberger, Bilech, and Orttung⁵ reported that this thiol, a very insoluble, yellow powder melting at 288–298°, could be obtained nearly quantitatively by reducing 4-chlorosulfonylcinnamic acid

with stannous chloride and hydrogen chloride in acetic acid.

The discrepancy in the reported properties of 4-mercaptocinnamic acid prompted us to synthesize this substance by other procedures. Cinnamic acid could be conveniently chlorosulfonated exclusively in the *para* position with chlorosulfonic acid.^{6,7} This sulfonyl chloride (I) was subjected to hydriodic acid reduction conditions,⁷ and a crude disulfide obtained. The extreme insolubility of this disulfide complicated the purification, so the crude material was subjected to zinc and acetic acid reduction,⁸ and the thiol (III) was obtained in good yield, with a melting point of 212–215°. Attempts at recrystallizing this thiol led to oxidation, as evidenced by a melting point above 300° of the recrystallized product. It was satisfactorily purified by sublimation under vacuum to give a faintly yellow powder which melted at 217–218° and analyzed correctly for III. The thiol III was oxidized with iodine in



ethanol to the disulfide II. This purified disulfide is an insoluble, faintly yellow powder, melting at 307–308°.⁹

Overberger⁵ reported the acetylation of the product obtained by reducing the sulfonyl chloride (I) with stannous chloride and hydrogen chloride to give a thiolacetate melting at 218–219°. 4-Mercaptocinnamic acid (III) was subjected to the same acetylation conditions and gave yellow needles, melting at 222–223°, whose infrared spectrum and

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(2) Taken from a portion of a thesis submitted by W. W. M. in partial fulfillment of the requirements for the degree Doctor of Philosophy at Indiana University, September, 1961.

(3) E. Campaigne and R. E. Cline, *J. Org. Chem.*, **21**, 32 (1956).

(4) T. Kurihara and H. Niwa, *J. Pharm. Soc. Japan*, **72**, 700 (1952); *Chem. Abstr.*, **47**, 3271e (1953).

(5) C. G. Overberger, H. Bilech, and F. W. Orttung, *J. Org. Chem.*, **24**, 289 (1959).

(6) J. Stewart, *J. Chem. Soc.*, **121**, 2555 (1922).

(7) A. H. Weinstein, R. M. Pierson, B. Wargotz, and T. F. Yen, *J. Org. Chem.*, **23**, 363 (1958).

(8) C. F. H. Allen and D. D. MacKay, *Org. Syntheses*, Coll. Vol. II, 580 (1943).

(9) In their various attempts at synthesizing 4-mercaptocinnamic acid, Overberger and co-workers⁵ observed the formation of a minor product, melting at 210–211°, which they suggested might be the *cis* isomer, but which was not fully characterized. It may actually have been impure *p*-mercaptocinnamic acid (III).

TABLE I
 PROPERTIES OF *p*-MERCAPTOCINNAMIC ACID AND DERIVATIVES

Compound	M.p., °C.		Formula	Sulfur, %	
	Found	Literature		Calcd.	Found
4-HSC ₆ H ₄ CH=CHCOOH	217-218	288-290 ^a 95-96 ^b	C ₉ H ₉ O ₂ S	17.80	17.66
4-CH ₃ COSC ₆ H ₄ CH=CHCOOH	222-223	218 ^a	C ₁₁ H ₁₀ O ₃ S	14.43	14.32
4-HSC ₆ H ₄ CH=CHCOOCH ₃	80-81		C ₁₀ H ₁₀ O ₂ S	16.51	16.19
4-C ₂ H ₅ SC ₆ H ₄ CH=CHCOOH	163-168		C ₁₁ H ₁₂ O ₂ S	15.39	15.04
4-C ₂ H ₅ SC ₆ H ₄ CH=CHCOOCH ₃	72-73		C ₁₂ H ₁₄ O ₂ S	14.42	14.45
(SC ₆ H ₄ CH=CHCOOH-4) ₂	306-307		C ₁₈ H ₁₄ O ₄ S ₂	17.89	17.64
(-SC ₆ H ₄ CH=CHCOOCH ₃ -4) ₂	134-135		C ₂₀ H ₁₈ O ₄ S ₂	16.59	16.33

^a C. G. Overberger, H. Bilech, and F. W. Orttung, *J. Org. Chem.*, **24**, 289 (1959). ^b T. Kurihara and H. Niwa, *J. Pharm. Soc. Japan*, **72**, 700 (1952); *Chem. Abstr.*, **47**, 3271e (1953).

 TABLE II
 PROPERTIES OF *p*-MERCAPTobenzoic ACID AND DERIVATIVES

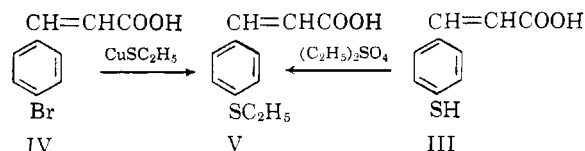
Compound	M.p., °C.		Formula	Sulfur, %	
	Found	Literature		Calcd.	Found
4-HSC ₆ H ₄ COOH	216-217	219 ^a	C ₇ H ₆ O ₂ S	20.79	20.91
4-HSC ₆ H ₄ COOCH ₃	52-53	55-56 ^b	C ₈ H ₆ O ₂ S	19.06	18.67
4-CH ₃ SC ₆ H ₄ COOH	191-192	190-192 ^c	C ₈ H ₈ O ₂ S	19.06	18.61
4-CH ₃ SC ₆ H ₄ COOCH ₃	80-80.5	82 ^a	C ₉ H ₁₀ O ₂ S	17.59	17.56
(-SC ₆ H ₄ COOH-4) ₂	326-328	327-330 ^d	C ₁₄ H ₁₀ O ₄ S ₂	20.93	20.12
(-SC ₆ H ₄ COOCH ₃ -4) ₂	125-126	124-125 ^d	C ₁₆ H ₁₄ O ₄ S ₂	19.18	19.26

^a K. Brand and O. Stallman, *J. prakt. Chem.*, **107**, 358 (1924); *Chem. Abstr.*, **18**, 2513 (1924). ^b L. Katz, L. S. Karger, W. Schroeder, and M. S. Cohen, *J. Org. Chem.*, **18**, 1380 (1953). ^c S. Smiles and D. C. Harrison, *J. Chem. Soc.*, **121**, 2022 (1922). ^d L. Schotte, *Arkiv. Kemi*, **9**, 299 (1956).

analyses confirm the thiolacetate structure. The disulfide (II) was subjected to similar acetylation conditions and the identical thiolacetate was obtained.

The infrared spectra of the thiol (III) and its derivatives all exhibit strong bands at 980 cm.⁻¹. This band has been attributed to the carbon-hydrogen bending in *trans*-symmetrically disubstituted ethylenes^{10,11} indicating the *trans* configuration around the double bond of these cinnamic acid derivatives.

In order to alleviate any question as to the structural assignment of the thiol III, it was desired to synthesize the *p*-mercaptocinnamic acid system by another independent route. Recently Adams, *et al.*,^{12,13} have published procedures by which aryl halides may be displaced by cuprous mercaptides. This technique would potentially lead to a *p*-alkylmercaptocinnamic acid which could be compared with the same derivative of the thiol III. *p*-Bromocinnamic acid (IV) was obtained and subjected to reaction with cuprous ethylmercaptide to produce the desired *p*-ethylmercaptocinnamic acid (V) in good yields. This product (V) was identical in all respects to that obtained by alkyl-



(10) R. S. Rasmussen and R. B. Brattain, *J. Chem. Phys.*, **15**, 131 (1947).

(11) M. S. C. Fleet, *J. Chem. Soc.*, 962 (1951).

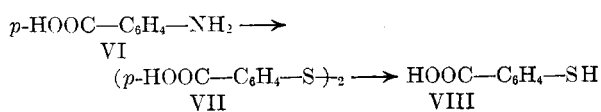
(12) R. Adams, W. Reifschneider, and M. D. Nair, *Croat. Chem. Acta*, **29**, 277 (1957).

(13) R. Adams and A. Ferretti, *J. Am. Chem. Soc.*, **81**, 4972 (1959).

ating *p*-mercaptocinnamic acid (III) with diethyl sulfate in alkali.

p-Mercaptocinnamic acid, 4,4'-dithiobiscinnamic acid, and *p*-ethylmercaptocinnamic acid were each esterified by standard techniques. All of these compounds are new and their physical properties are tabulated in Table I.

The analogous benzoic acid derivatives were also desired for the ultraviolet spectral work. The parent compound, *p*-mercaptobenzoic acid, was obtained from the corresponding amino acid. The diazonium salt of the amine (VI) was treated with sodium disulfide to give a crude 4,4'-dithiobisbenzoic acid (VII), which, due to its extreme insolubility, was very difficult to purify. Reduction of this crude disulfide with zinc and acetic acid gave *p*-mercaptobenzoic acid (VIII) in good yields. As with the case of the cinnamic acid analog (III), this mercapto acid was impossible to purify by recrystallization, because of its facile oxidation to the disulfide. Excellent purification was obtained, however, by sublimation under vacuum. The remaining benzoic acid derivatives were prepared by standard techniques and their properties are listed in Table II.



Discussion of the Absorption Spectra

The ultraviolet absorption spectra of the cinnamic and benzoic acid derivatives were obtained on a Cary Model 14 recording spectrophotometer,

equipped with a hydrogen discharge tube and 1-cm. silica cells. The spectral characteristics were observed over a wave length range of 400–210 $m\mu$. The compounds were recrystallized immediately before the spectra were determined and fresh solutions of about 5×10^{-6} moles/l. were used in each instance.

Previously, advantage has been taken of the possibility of determining the spectra of various acidic substances of this type in neutral and in alkaline solutions.³ The spectra of the compounds involved in the present study were determined in 95% ethanol solution as a neutral system. Alcoholic potassium acetate solutions were also used for the spectral determinations in the hope of affecting essentially complete ionization of the free carboxyl groups without ionization of the thiol groups. This would allow one to study the spectral shifts due to the ionization of a carboxyl group in the presence of an unionized thiol function. Finally, the spectra were determined in alcoholic potassium hydroxide solution in order to ascertain the spectral effects of completely ionizing both the carboxyl and thiol groups.

The spectra were initially determined on freshly prepared solutions in 95% ethanol. At the completion of the runs, a standard drop (0.05 ml.) of 10% aqueous potassium acetate was added directly to the sample cell and the reference cell and the spectra were immediately re-recorded. This brought about a concentration of acetate of about 5×10^{-4} moles/l., a 10 molar excess over the concentration of the compound being studied. At the end of the determinations in potassium acetate solution, 0.05 ml. of 10% aqueous potassium hydroxide was added immediately to each cell and the spectra recorded again. The potassium hydroxide was also present in ten times the concentration of the acidic substance being ionized, leading to complete ionization of the carboxyl and thiol functions. The absorption maxima and their extinction coefficients of the cinnamic acid and benzoic acid derivatives are listed in Tables III and IV, respectively.

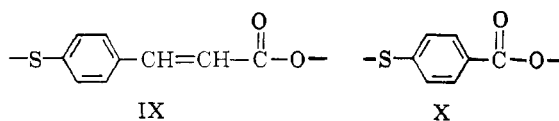
The spectra, in neutral solution, of the compounds included in this study exhibit absorption peaks of two different types. Very intense peaks are observed between 303 and 328 $m\mu$ for the cinnamic acid series and between 271 and 292 $m\mu$ for the benzoic acid derivatives. The second type of absorption is indicated by lower wave length peaks about one-half as intense as the peaks of the first type. These peaks are found between 226 and 252 $m\mu$ for the cinnamic acids and 215 and 240 $m\mu$ for the benzoic acids.

The intense longer wave length peaks are characteristic of the conjugated systems, IX and X, and indicate the powerful conjugation between the sulfur and carboxyl functions through the benzene system in the benzoic acids and the styrene system in the cinnamic acids,^{3,14–16}

TABLE III
ULTRAVIOLET ABSORPTION MAXIMA AND MOLAR EXTINCTION COEFFICIENTS OF *p*-MERCAPTOCINNAMIC ACID DERIVATIVES

Compound ^b	Solvent	Maxima ^a			
		$\lambda(m\mu)$	ϵ		
4-HSC ₆ H ₄ CH=CHCOOH	95% C ₂ H ₅ OH	(315)	20,800		
		307	21,200		
		230	10,800		
	KOAc	353	14,000		
		315	11,100		
		307	11,300		
		295	11,300		
		KOH	353	23,700	
		240	10,500		
4-HSC ₆ H ₄ CH=CHCOOCH ₃	95% C ₂ H ₅ OH	315	20,000		
		(307)	19,700		
		229	13,200		
	KOAc	387	21,300		
		(315)	7,600		
		252	10,800		
	KOH	387	22,100		
		252	11,000		
		230	11,200		
4-C ₂ H ₅ SC ₆ H ₄ -CH=CHCOOH	95% C ₂ H ₅ OH	323	21,600		
		237	10,400		
		300	20,800		
	KOAc	230	11,700		
		KOH	300	20,500	
		230	11,200		
	4-C ₂ H ₅ SC ₆ H ₄ -CH=CHCOOCH ₃	95% C ₂ H ₅ OH	328	22,000	
			239	10,100	
			KOAc	328	22,000
KOH		239	10,100		
		328	22,000		
		239	10,100		
(—SC ₆ H ₄ CH=CHCOOH- ₄) ₂		95% C ₂ H ₅ OH	303	34,300	
			226	19,900	
			KOAc	293	35,200
	KOH	293	35,400		
		(—SC ₆ H ₄ CH=CHCOOCH ₃ - ₄) ₂	95% C ₂ H ₅ OH	319	41,400
				230	21,300
	KOAc			319	41,400
	KOH		230	21,300	
			319	40,700	
230			21,300		

^a The wave lengths in parentheses refer to inflection points. ^b Source: see section on "Preparation of Compounds."



The lower wave length peaks of the second type have been ascribed to excitation of the nonbonding electrons of the highly polarizable sulfur atoms.^{17,18} Absorption bands due to this type of excitation, such as those characteristic of dialkyl sulfides, often absorb at 210 $m\mu$ or below.^{18,19} However, the groups attached to the sulfur atoms in this study are capable of providing influences either inductive

- (14) L. Schotte, *Arkiv Kemi*, **9**, 299 (1956).
 (15) C. C. Price and J. J. Hydock, *J. Am. Chem. Soc.*, **74**, 1943 (1952).
 (16) J. W. Baker, G. F. C. Barrett, and W. T. Tweed, *J. Chem. Soc.*, 2834 (1952).
 (17) R. S. Mulliken, *J. Chem. Phys.*, **3**, 506 (1935).
 (18) E. A. Fehnel and M. Carmack, *J. Am. Chem. Soc.*, **71**, 84 (1949).
 (19) H. P. Koch, *J. Chem. Soc.*, 387 (1949).

TABLE IV

ULTRAVIOLET ABSORPTION MAXIMA AND MOLAR EXTINCTION COEFFICIENTS OF 4-MERCAPTOBENZOIC ACID DERIVATIVES

Compound	Source ^a	Solvent	Maxima		
			$\lambda(m\mu)$	ϵ	
4-HSC ₆ H ₄ COOH	1	95% C ₂ H ₅ OH	272	16,700	
			218	8,850	
			314	8,450	
			263	8,650	
			309	18,000	
4-HSC ₆ H ₄ CO-OCH ₃	2	95% C ₂ H ₅ OH	274	16,300	
			220	8,550	
			333	20,000	
		KOAc	240	5,450	
			KOH	333	21,000
			240	5,450	
4-CH ₃ SC ₆ H ₄ -COOH	3	95% C ₂ H ₅ OH	289	17,200	
			224	8,100	
			274	15,600	
		KOAc	215	8,800	
			KOH	274	16,100
			223	5,400	
4-CH ₃ SC ₆ H ₄ -COOCH ₃	4	95% C ₂ H ₅ OH	292	20,000	
			225	8,000	
			292	20,000	
		KOAc	225	8,000	
			KOH	292	19,600
			225	7,400	
(—SC ₆ H ₄ CO-OH-4) ₂	5	95% C ₂ H ₅ OH	271	21,800	
			KOAc	261	21,400
			KOH	261	21,000
(—SC ₆ H ₄ CO-OCH ₃ -4) ₂	6	95% C ₂ H ₅ OH	275	26,000	
			KOAc	275	26,000
			KOH	275	23,500

^a Source references: (1) see section on "Preparation of Compounds;" (2) L. Katz, L. S. Karger, W. Schroeder, and M. S. Cohen, *J. Org. Chem.*, **18**, 1380 (1953); (3) Prepared by methylating the corresponding thiol with dimethyl sulfate in alkali; (4) N. B. Lorette and J. H. Brown, Jr., *J. Org. Chem.*, **24**, 261 (1959); (5) Prepared by oxidizing the corresponding thiol with iodine in ethanol; (6) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green, and Co., London, 3rd ed., 1956, p. 784.

or conjugative in nature such that these peaks can be shifted bathochromically as observed in the tables of spectral data. For example, alkylation of the thiol groups causes bathochromic shifts of these lower wave length peaks of 6 to 7 $m\mu$ due to the inductive effects of the alkyl groups. Ionization of the thiol groups causes similar shifts of 10 to 45 $m\mu$.

The spectra of all the compounds measured show strong absorption in the far ultraviolet (below 210 $m\mu$). This phenomenon is characteristic of aromatic compounds, carbonyl derivatives, and sulfides, all of which are present in the compounds studied.

The general spectral characteristics of these compounds are in agreement with predictable values. Cinnamic acid absorbs strongly at 275 $m\mu$ ²⁰ while benzoic acid exhibits an intense band near 232 $m\mu$.²¹ The absorption maxima at 315 and 307 $m\mu$ for 4-mercaptocinnamic acid and at 272 $m\mu$ for 4-mercaptobenzoic acid are in accord with the pre-

dicted shift associated with the addition of —SH to a conjugated system.²² A bathochromic shift of the principal absorption maximum accompanies the conversion of a carboxylic acid to its methyl ester. In the benzoic acid derivatives this shift is 2–4 $m\mu$ while it ranges from 5–16 $m\mu$ for the cinnamic acid analogs. A bathochromic shift of 15 ± 3 $m\mu$ is observed as each thiol group is alkylated. These shifts are attributed to the inductive effects of the alkyl groups. The slight hypsochromic shift accompanying the conversion of a thiol to its corresponding disulfide is in accord with earlier observations in this laboratory.^{3,23} These data support the assumption that the disulfide bond does not add conjugation to the system. This is exemplified by absorption maxima which are not shifted bathochromically and by absorption intensities nearly double those of the individual chromophores.

The various shifts accompanying the determination of the spectra in alkaline solutions are both interesting and significant. The graphical representations of the typical shifts observed, as the carboxyl group alone, the thiol group alone, and when both the carboxyl and thiol groups are ionized, are indicated in Fig. 1, 2, and 3, respectively.

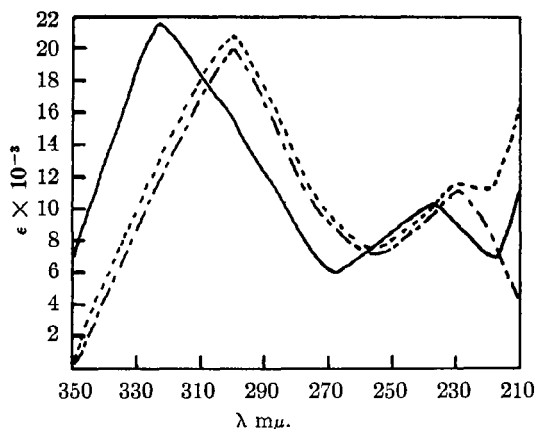


Fig. 1.—Absorption spectra of 4-ethylmercaptocinnamic acid; in 95% ethanol solution —; in ethanolic potassium acetate solution ----; in ethanolic potassium hydroxide solution —.—.

A relatively constant hypsochromic shift of 10 ± 2 $m\mu$ is associated with the ionization of a carboxyl group. These data agree closely with earlier reports on similar types of molecules.³ The alkylmercapto acids provide the only exceptions to this observation. The hypsochromic shift from ionizing 4-methylmercaptobenzoic acid is 15 $m\mu$ while that associated with the ionization of 4-ethylmercaptocinnamic acid is 23 $m\mu$.

A huge bathochromic shift is observed as the free thiol groups of the mercapto esters are ionized. This shift amounts to 59 $m\mu$ for methyl 4-mercapto-

(20) S. Bodfors, *Ann.*, **534**, 235 (1938).

(21) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N.Y., 1951, p. 71.

(22) K. Bowden, E. A. Braude, and E. R. H. Jones, *J. Chem. Soc.*, **948** (1946).

(23) E. Campaigne, J. Tsurugi, and W. W. Meyer, *J. Org. Chem.*, **26**, 2486 (1961).

benzoate and 72 $m\mu$ for methyl 4-mercaptocinnamate. When the spectra of the mercapto acids are measured in potassium hydroxide where both acidic functions are ionized, the moderate hypsochromic effect of ionizing the carboxyl groups and the larger bathochromic shifts accompanying ionization of the thiol groups counteract one another, so the net effect is a smaller bathochromic shift (27 $m\mu$ for 4-mercaptobenzoic acid and 46 $m\mu$ for 4-mercaptocinnamic acid).

The spectra determined in potassium acetate solution indicate that the carboxyl groups are completely ionized and that the thiol groups are partially ionized. Even so, it is possible to observe the various shifts as the carboxyl and thiol groups are selectively ionized. For example the spectrum of 4-mercaptocinnamic acid in potassium acetate solution exhibits the peaks characteristic of the ionization of neither acidic group (315 $m\mu$ and 307 $m\mu$), the ionization of both acidic groups (353 $m\mu$), and the ionization of the carboxyl group alone (295 $m\mu$). There is an anomaly in the spectra of *p*-mercaptobenzoic acid. The peak characteristic of the ionization of both acidic groups shifts from 314 $m\mu$ to 309 $m\mu$ as the potassium hydroxide is added to the potassium acetate. This peak remains stationary under similar conditions in the other molecules.

From the tables of spectral data, it is apparent that the thiol groups are rather highly ionized in acetate solution, especially in the case of the mercapto esters. This would indicate that these thiol groups exhibit acid strengths almost as great as those of the carboxyl groups. To put this phenomenon on a more quantitative basis, the pK_a values of the two mercapto esters and the two mercapto acids were obtained and compared with those of benzoic acid, cinnamic acid, and benzenethiol. The results are tabulated in Table V.

TABLE V

pK_a VALUES OF BENZOIC AND CINNAMIC ACID DERIVATIVES IN 60% ETHANOL AT 22°

Compound	pK_a
C_6H_5COOH	5.9
$C_6H_5CH=CHCOOH$	6.0
C_6H_5SH	8.0
4-HSC ₆ H ₄ COOCH ₃	6.5
4-HSC ₆ H ₄ COOH	6.0
	7.6
4-HSC ₆ H ₄ CH=CHCOOCH ₃	6.9
4-HSC ₆ H ₄ CH=CHCOOH	6.1
	7.7

The pK_a of benzoic acid agrees very closely with the reported value for the same solvent system.²⁴ These pK_a data indicate that methyl *p*-mercaptobenzoate and methyl *p*-mercaptocinnamate are considerably stronger acids than benzenethiol and their acid strengths are within one pK_a unit of those of benzoic and cinnamic acids. Therefore, there is good reason for a significant degree of

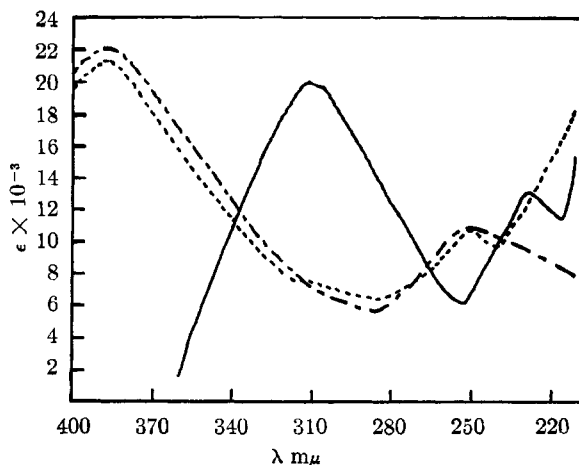


Fig. 2.—Absorption spectra of methyl 4-mercaptocinnamate; in 95% ethanol solution —; in ethanolic potassium acetate solution ---; in ethanolic potassium hydroxide solution -.-.-.

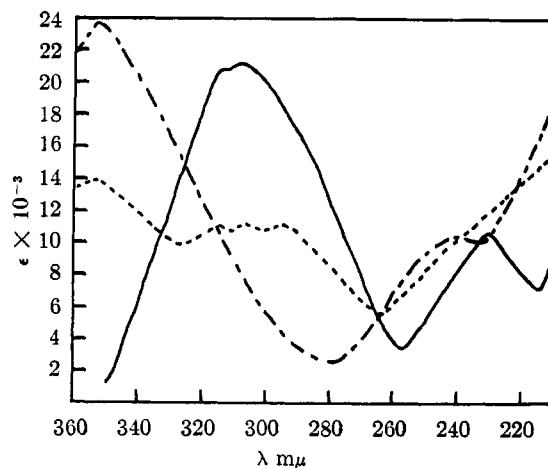
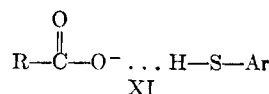


Fig. 3.—Absorption spectra of 4-mercaptocinnamic acid; in 95% ethanol solution —; in ethanolic potassium acetate solution ---; in ethanolic potassium hydroxide solution -.-.-.

ionization of the thiol groups of the mercapto esters in alcoholic potassium acetate solution.

The spectral data indicate that the corresponding thiol groups of the mercapto acids are ionized to a lesser degree in acetate solution. The pK_a data of these compounds indicate the stepwise ionization of the two acidic functions. The pK_a values of the carboxyl groups of *p*-mercaptobenzoic (6.0) and *p*-mercaptocinnamic (6.1) acids are very near those of the unsubstituted parent acids. This may be explained by assuming that the acid-weakening effect due to the electron-releasing nature of the *para*-thiol group is nearly neutralized by an acid-strengthening effect resulting from the stabilization of the carboxylate anion by its inter-



molecular association with the hydrogen of another thiol group.

This hydrogen bonding (XI) also accounts for the observation that the acid strengths of the thiols of the mercapto acids are greatly reduced compared to those of the corresponding mercapto esters, since ionization of the thiols occurs after the carboxyl functions are ionized. The acid-weakening effect due to the conjugation of a *para*-carboxylate ion also helps account for this phenomenon.

Experimental²⁵

p*K*_a Determinations.—The p*K*_a values were obtained by titrating each compound in 60% ethanol (by volume) at 22° with standard sodium hydroxide. The pH readings were obtained on a Tadiometer Titrator, Type TTT la pH meter and were recorded manually.

***p*-Mercaptocinnamic Acid.**—The hydriodic acid reduction procedure used is a modification of a general one.⁷ Twenty grams (0.08 mole) of *p*-chlorosulfonylcinnamic acid⁸ was suspended in 400 ml. of glacial acetic acid. The mixture was stirred and 75 ml. of 47% hydriodic acid was added. Stirring was maintained for 4 hr. whereupon the reaction was allowed to stand overnight. The dark, viscous reaction mixture was then poured into a solution of 105 g. of sodium thiosulfate in 700 ml. of water in order to decolorize it. The yellow precipitate was collected and reprecipitated from 10% sodium hydroxide solution with dilute acid. The yield of crude 4,4'-dithiobiscinnamic acid was 15 g. (100%), m.p. 250–270° dec.

A procedure based on a report of Allen and MacKay⁸ was used for the zinc and acetic acid reduction. Into a 300-ml. three-necked flask fitted with a motor-driven Teflon stirrer and reflux condenser was placed a mixture of 3.6 g. (0.01 mole) of crude 4,4'-dithiobiscinnamic acid and 2.5 g. of zinc dust suspended in 50 ml. of glacial acetic acid. The mixture was stirred *vigorously* under reflux for 10 hr. during which time several additional 1-g. portions of zinc dust were added. The light gray solid material was collected by suction, washed in 100 ml. of hot water, and placed in another 100 ml. of hot water to which was added a solution of 5 g. of sodium hydroxide in 20 ml. of water. The alkaline solution was stirred for 5 min. and filtered with suction to remove the insoluble impurities. The filtrate was then acidified with concentrated hydrochloric acid and the precipitated white solid collected by suction, pressed as dry as possible, and dried in a vacuum desiccator over potassium hydroxide. The yield of crude material was 2.2 g. or 61%, m.p. 212–215°. A sample was sublimed at 210° and 0.1 mm. pressure to give a faintly yellow powder, m.p. 217–218°.

Acetylation of *p*-Mercaptocinnamic Acid.—The procedure of Overberger⁸ was modified slightly. A sample of 0.9 g. (0.005 mole) of *p*-mercaptocinnamic acid (m.p. 217–218°) in 25 ml. of 20% aqueous potassium hydroxide was cooled and treated with 5 g. (0.05 mole) of acetic anhydride in small portions. The reaction mixture was swirled vigorously after each addition and cooled in ice water to maintain the temperature below 40°. An instantaneous precipitation of white solid accompanied the addition of the last portion of the anhydride. Seven milliliters of 6 *N* hydrochloric acid was then added to ensure complete precipitation and the white solid (0.9 g., 81%) collected and dried. Several recrystallizations from dilute ethanol gave light yellow needles, m.p. 222–223°.

***p*-Bromocinnamic Acid.**—To a mixture of 150 ml. of pyridine and 2.5 ml. of piperidine in a 1000-ml. flask was added 46.3 g. (0.25 mole, m.p. 57–59°) of *p*-bromobenzaldehyde and 78 g. (0.75 mole) of malonic acid. The flask was

fitted with a reflux condenser and the reaction mixture heated on a steam bath for 3 hr. A steady evolution of carbon dioxide was observed throughout the reaction period. After cooling, the reaction mixture was poured with stirring into 1000 ml. of water containing 150 ml. of concentrated hydrochloric acid. The resulting white, soupy mass was collected and dried. The crude material (53.1 g., 94%) melted at 255–259°. The product was recrystallized several times from 95% ethanol to give fine, white needles, m.p. 258–260°. The reported melting point is 257°. ²⁸

***p*-Ethylmercaptocinnamic Acid.**—Procedure A is an adaptation of the general procedure of Adams and Ferretti.¹³ A mixture of 22.7 g. (0.1 mole) of *p*-bromocinnamic acid, 13.5 g. (0.108 mole) of cuprous ethylmercaptide prepared as described,¹³ 100 ml. of quinoline, and 8 ml. of pyridine was placed in a flask fitted with a thermometer, air-reflux condenser, and magnetic stirrer. The dark brown solution was heated with stirring to 200° for 9 hr. No visible changes could be observed during this period. The solution was then poured over ice water containing an excess of hydrochloric acid and the mixture allowed to stand overnight. The dark brown solid was collected and transferred to a flask where it was extracted with 600 ml. of boiling chloroform for 5 hr. The insoluble impurities were removed and the filtrate concentrated to give 7.2 g. or 35% of light yellow plates, m.p. 162–168°. The product was recrystallized several times from dilute ethanol to give long, white needles, m.p. 163–168°.

Procedure B. A 0.65-g. sample of pure *p*-mercaptocinnamic acid was dissolved in 10 ml. of 10% sodium hydroxide at 50°. Dropwise addition of 1.5 g. of diethyl sulfate to the stirred solution gave a curdled precipitate which dissolved on dilution to 200 ml. Acidification yielded 0.6 g. (52%) of fluffy white crystals, melting at 163–167° after recrystallization as needles from ethanol. A mixture melting point with the product of procedure A was undepressed, and infrared spectra were superimposable.

***p*-Ethylmercaptocinnamide.**—Treatment of 1.04 g. of *p*-ethylmercaptocinnamic acid with thionyl chloride, followed by aqueous ammonia, gave 0.5 g. of white prisms of the amide melting at 163–165°.

Anal. Calcd. for C₁₁H₁₃ONS: N, 6.76; S, 15.47. Found: N, 6.70; S, 15.31.

Methyl *p*-Mercaptocinnamate.—The procedure was based on that described by Katz and co-workers.²⁷ A sample of pure *p*-mercaptocinnamic acid (0.9 g., 0.005 mole) in 50 ml. of absolute methanol was saturated with dry hydrogen chloride gas. The warm solution was then gently refluxed for 3 hr., poured into ice water, and the solid materials taken up in ether. The ether layer was washed with saturated sodium bicarbonate solution, water, and dried over anhydrous sodium sulfate. The ether was then removed under diminished pressure leaving 0.85 g. (80%) of a light yellow solid melting at 72–78°. A sample was recrystallized from *n*-pentane as white aggregates, m.p. 80–81°.

4,4'-Dithiobiscinnamic Acid.—A solution of iodine in ethanol was added dropwise to a solution of 1.8 g. (0.01 mole) of *p*-mercaptocinnamic acid in 100 ml. of 95% ethanol until the iodine color persisted. The precipitated yellow solid (1.52 g., 85%) was collected and dried. Small samples could be recrystallized from dioxane to give light yellow aggregates, m.p. 306–307°.

A cooled solution of 0.9 g. (0.0025 mole) of this disulfide in 25 ml. of 20% aqueous potassium hydroxide was treated with 5 g. of acetic anhydride, as described for the acetylation of *p*-mercaptocinnamic acid, and 0.7 g. (57%) of product was obtained. This compound was recrystallized from dilute ethanol as light yellow needles, melting at 222–223°. A mixed melting point with *p*-thioacetoxycinnamic acid was

(26) I. Heilbron, "Dictionary of Organic Compounds," Vol. I, Oxford University Press, New York, N. Y., 1953, p. 317.

(27) L. Katz, L. S. Karger, W. Schroeder, and M. S. Cohen, *J. Org. Chem.*, **18**, 1380 (1953).

(25) Microanalyses were performed by Midwest Microlab, Inc. All melting points are corrected.

undepressed, and the infrared spectra of these two products were superimposable.

Dimethyl 4,4'-Dithiobiscinnamate.¹³—Into a three-necked flask fitted with a gas-inlet tube and reflux condenser were placed 0.5 g. (0.0014 mole) of 4,4'-dithiobiscinnamic acid and 50 ml. of absolute methanol. A gentle stream of dry hydrogen chloride gas was introduced into the mixture for 12 hr. accompanied by gentle refluxing. The insoluble material was removed and the filtrate concentrated. The isolated solid product was washed with warm 5% aqueous sodium bicarbonate and recrystallized from dilute ethanol to give 0.1 g. (20%) of white plates, m.p. 134–135°.

Methyl *p*-Ethylmercaptocinnamate.—Using a reported general procedure,²⁸ *p*-ethylmercaptocinnamic acid (1.04 g. 0.005 mole) was treated with thionyl chloride, and the excess thionyl chloride removed under diminished pressure, leaving a residual yellow oil. About 25 ml. of absolute methanol was then carefully added to the residue and this mixture refluxed for 3 hr. The product crystallized from the reaction mixture to give 0.9 g. (81%) of crude product, m.p. 65–70°. The material was recrystallized several times from dilute ethanol to give white plates, m.p. 72–73°.

***p*-Mercaptobenzoic Acid.**—A convenient modification of the procedure of Allen and MacKay⁸ was used. A mixture of 290 ml. of water, 260 g. (1.1 moles) of crystallized sodium sulfide ($\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$), and 34 g. of powdered elemental sulfur was placed in a 4-l. beaker and warmed to effect solution. A solution of 40 g. of sodium hydroxide pellets in 100 ml. of water was then added and the mixture cooled in an ice bath to 5°. Into a 2-l. beaker, set in an ice bath and provided with a stirrer and a thermometer, were placed 500 ml. of water, 137 g. (1.0 mole, Eastman Practical Grade) of *p*-aminobenzoic acid, and 200 ml. of concentrated hydrochloric

acid. When the temperature of the mixture had fallen to 5°, a solution of 69 g. (1.0 mole) of sodium nitrite in 280 ml. of water was added from a dropping funnel whose tip extended below the surface of the liquid. The addition required about 15 min. and cracked ice was added to keep the temperature below 5°. The stirrer was then transferred to the alkaline sulfide solution and the diazonium salt solution added over a 0.5-hr. period, keeping the temperature below 5°. The mixture was allowed to warm slowly to room temperature accompanied by the evolution of nitrogen gas. The solution was made acid to Congo red paper with 180 ml. of concentrated hydrochloric acid and the precipitated, crude disulfide collected with suction. The product was reprecipitated from warm 10% aqueous sodium carbonate solution, collected, and dried in the air, giving 150 g. (98%) of crude material, m.p. 315–320°.

A mixture of crude 4,4'-dithiobisbenzoic acid (31 g., 0.1 mole) and 20 g. of zinc dust was suspended in 250 ml. of glacial acetic acid in a flask fitted with a motor-driven stirrer and a reflux condenser. The reaction mixture was stirred vigorously under reflux for 6 hr. Several additional small portions of zinc dust were added during this period. The solid materials were collected by suction, washed in 250 ml. of hot water, recollected, and placed into 250 ml. of hot water to which was added a solution of 25 g. of sodium hydroxide pellets in 50 ml. of water. The alkaline solution was heated for about 5 min., filtered to remove the insoluble impurities, and the filtrate acidified immediately. The white product was collected, pressed as dry as possible, and dried in a vacuum desiccator over potassium hydroxide. The yield was 21 g. or 68%, m.p. 216–219°. A sample was sublimed at 205° and 0.1 mm. pressure to give a white powder, m.p. 216–217°. The reported melting point is 219°.²⁹

(28) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green, and Co., London, 3rd ed., 1956, p. 784.

(29) I. Heilbron, "Dictionary of Organic Compounds," Vol. III, Oxford University Press, New York, N. Y., 1953, p. 248.

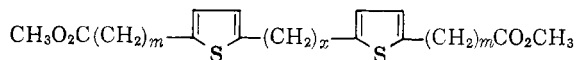
An Investigation of Some Approaches to the Synthesis of α -Cyclodipolymethylenedithiophenes

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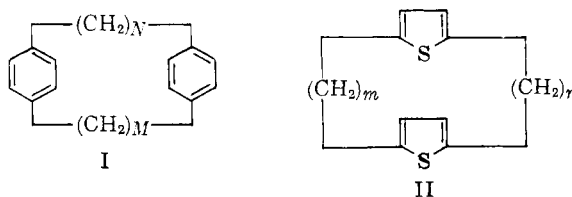
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Esters having the general structure,



($x = 1, m = 3$; $x = 1, m = 5$; $x = 6, m = 2$; and $x = 6, m = 3$), were synthesized from thiophene and subjected to high dilution intramolecular acyloin condensations in an attempt to prepare thiophene analogs (II) of the paracyclophanes. In all cases studied, no evidence for a cyclic structure was obtained. However, a linear acyloin, 3-hydroxy-4-keto-1,6-bis(2'-thienyl)hexane, could be obtained from ethyl β (2-thienyl)propionate.

The investigation reported here was partially suggested by the study of Cram and his collaborators³ on the properties of cyclic molecules involving benzene rings, the paracyclophanes (I). These compounds were shown to possess unusual chemical and physical properties,³ due to modification of the



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(3) D. J. Cram, W. J. Wechter, and R. W. Kurstead, *J. Am. Chem. Soc.* **80**, 3126 (1958) and references cited.

benzenoid resonance resulting from bowing of the benzene rings toward one another, to transannular effects, and to restricted rotation of the benzene