in 50 ml. of hot water was neutralized to *p*H 7 with concentrated ammonium hydroxide. The solution was concentrated under vacuum on the steam-bath until a precipitate began to form. The mixture was cooled in an ice-bath and the precipitate collected. Two crops yielded 0.84 g. (100%), m.p. 237–242° dec.

2-Methylphenylalanine (II).—A suspension of 33.5 g. (0.11 mole) of IIa in 400 ml. of 20% hydrobromic acid was refluxed for 6 hr., and the solution was concentrated under vacuum on the steam-bath until a solid began to form. The mixture was cooled in an ice-bath and the crystals collected by filtration; yield 21.0 g. (78%). A solution of 18.0 g. (0.069 mole) of the amino acid hydrobromide in 200 ml. of water was added to an aqueous slurry of 70.0 g. of Amberlite IR-4B ion-exchange resin (basic form). The mixture was stirred and filtered and the resin washed with an additional 100 ml. of water. The combined filtrates were concentrated under vacuum until a precipitate formed. The solid which separated upon cooling in an ice-bath was collected. Two crops yielded 10.5 g. (85%), m.p. 240–243° dec.

KANKAKEE, ILLINOIS

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, THE ARMOUR LABORATORIES]

Analogs of Phenylalanine Containing Sulfur

BY ROBERT L. COLESCOTT, ROSS R. HERR AND JOSEPH P. DAILEY

RECEIVED DECEMBER 26, 1956

Analogs of phenylalanine containing a sulfur group in the *para* position have been synthesized and tested as growth inhibitors of *Escherichia coli*. The mercapto, symmetrical disulfide, methylmercapto, ethylmercapto, methylsulfinyl, methyl sulfonyl and sulfamyl analogs were prepared by hydrolysis and decarboxylation of the corresponding diethyl acylamidomalonates.

The substitution of various groups on the benzene ring of phenylalanine has often resulted in compounds that are competitive antagonists of phenylalanine or tyrosine, the *para* substituted compounds being the most active. Some of these *para* substituted analogs of phenylalanine that have been previously reported include the nitro,[1] amino,[1] fluoro,[2] chloro,[1] methyl,[3] dimethylamino,[4] mercapto,[5,6] sulfamyl[7,8] and the symmetrical disulfide.[5,6] Because of the potential usefulness of amino acid antagonists in chemotherapy, we have prepared a group of compounds related to phenylalanine wherein a sulfur containing group is substituted in the *para* position of this amino acid. In these compounds, variations in the oxidation state of the sulfur results in groups having a range of electronic effects, from the electron-donating mercapto group to the electron-withdrawing sulfonamide. In this way we hoped to obtain information about the relationship between electronic character of the substituent and antagonism or utilization of the amino acid. We have prepared the mercapto, disulfide, methylmercapto, ethylmercapto, methylsulfinyl, methylsulfonyl and sulfamyl substituted phenylalanines.

The general method of preparation of these amino acids was by way of the corresponding diethyl acetamidomalonate (Table I).

The amino acid was then prepared by hydrolysis and decarboxylation (Table II).

The preparation of *p*-mercaptophenylalanine was first reported by Johnson and Brautlecht[5] and later by Elliott and Harington.[6] A more direct route and one which resulted in higher yield was found in the reaction of potassium ethyl xanthate with diethyl *p*-diazobenzylacetamidomalonate. The diazo-compound was prepared readily from the corresponding amine and this, in turn, was obtained by hydrogenation of diethyl *p*-nitrobenzylacetamidomalonate.[1] The hydrolysis of the xanthate, the hydrolysis of the amide and ester groups, as well as the decarboxylation, were accomplished in one step to give the amino acid hydrochloride in 86% yield. Oxidation of the *p*-mercaptophenylalanine to the corresponding disulfide was carried out according to the procedure of Elliott and Harington using iodine in potassium iodide solution.

Chloromethylation of thioanisole or thioanethole with chloromethyl ether yielded the *para* substituted benzyl chloride. The thioanethole was prepared by the reaction of diethyl sulfate with thiophenol. Condensation of these benzyl halides with diethyl acetamidomalonate resulted in the production of the substituted acetamidomalonates which were then hydrolyzed and decarboxylated to yield *p*-methylmercaptophenylalanine and *p*-ethylmercaptophenylalanine.

Controlled oxidation of the diethyl *p*-methylmercaptobenzylacetamidomalonate with hydrogen peroxide resulted in the sulfinyl substituted malonate and hydrolysis of this yielded *p*-methylsulfinylphenylalanine. Oxidation with an excess of hydrogen peroxide gave the sulfone which was hydrolyzed to yield the corresponding sulfonyl amino acid.

Two methods were employed successfully in the preparation of *p*-sulfamylphenylalanine.[7] Chlorosulfonation of diethyl benzylacetamidomalonate followed by reaction with ethereal ammonia and hydrolysis and decarboxylation resulted in the sulfonamide in 16% yield. The alternate procedure utilized side chain bromination of *p*-toluene-

(1) J. B. Burckhalter and V. C. Stephens, THIS JOURNAL, **73**, 56 (1951).

(2) E. L. Bennett and C. Niemann, *ibid.*, **72**, 1800 (1950).

(3) J. G. Martin, R. Brendel and J. M. Beiler, *Exp. Med. & Surg.*, **8**, 5 (1950).

(4) D. F. Elliott, A. T. Fuller and C. R. Harington, *J. Chem. Soc.*, 85 (1948).

(5) T. B. Johnson and C. A. Brautlecht, *J. Biol. Chem.*, **12**, 175 (1912).

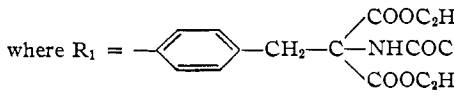
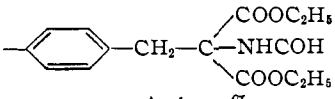
(6) D. F. Elliott and C. Harington, *J. Chem. Soc.*, 1374 (1949).

(7) J. C. Nevenzel, W. E. Shelberg and C. Niemann, THIS JOURNAL, **71**, 3024 (1949).

(8) This compound exhibited chemotherapeutic activity when evaluated in *Streptococcus hemolyticus* infected rabbits. C. Schaffer, *Proc. Soc. Exp. Biol. & Med.*, **37**, 648 (1937).

TABLE I

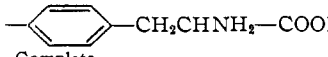
PHYSICAL PROPERTIES AND ANALYSES OF *para*-SULFUR SUBSTITUTED MALONATES

where R_1 =  and R_2 = 

Malonate	Empirical formula	Recrystallization solvent	M.p., °C.	Analyses, % Calcd. C	H	N	S	Cl	Found C	H	N	S	Cl
$C_2H_5OC(=S)-S-R_1$ (Ia)	$C_{19}H_{28}NO_6S_2$	70% Ethanol	103–105	53.40	5.85	3.28	15.00	..	53.48	5.83	3.19	14.96	..
CH_3S-R_1 (IIIa)	$C_{17}H_{21}NO_6S$	95% Ethanol	108.5–109.5	57.49	6.53	3.97	9.06	..	57.67	6.42	3.98	8.84	..
$C_2H_5S-R_1$ (IVc)	$C_{18}H_{25}NO_6S$	95% Ethanol	96–97	58.85	6.81	3.81	8.72	..	59.03	6.97	3.92	8.90	..
$CH_3C(=O)-R_1$ (Va)	$C_{17}H_{23}NO_6S$	Water	142–143	55.28	6.23	3.79	8.67	..	55.15	6.16	3.77	8.55	..
$CH_3S(=O)-R_1$ (VIa)	$C_{17}H_{23}NO_7S$	95% Ethanol	174–176	52.99	5.97	3.64	8.31	..	53.30	5.61	3.63	8 15	..
$ClSO_2-R_1$ (VIIa)	$C_{16}H_{20}ClNO_7S$	Chloroform–hexane	123–124	47.35	4.93	3.45	7.89	8.75	47.38	4.91	3.86	7.89	8.37
$NH_2SO_2-R_1$ (VIIb)	$C_{16}H_{22}N_2O_7S$	60% Methanol	240–241	49.69	5.70	7.25	8.28	..	49.76	5.61	7.14	8.09	..
$NH_2SO_2-R_2$ (VIIc)	$C_{16}H_{20}N_2O_7S$	Dioxane–hexane	239–240	48.40	5.37	7.80	8.61	..	48.43	5.57	7.36	8.78	..

TABLE II

PHYSICAL AND MICROBIOLOGICAL PROPERTIES OF *para*-SULFUR SUBSTITUTED PHENYLALANINES

where R = 

Amino acid	Empirical formula	M.p., °C. (dec.)	Complete inhibition of growth of *E. coli* γ/6 ml. media	Analyses, % Calcd. C	H	N	S	Found C	H	N	S
HS–R·HCl (I)	$C_9H_{11}NO_2S\cdot HCl$	248–249[f]	> 1,000[a,e]	...	..	...	...	...	..	...	...
R–S–S–R (II)	$C_{18}H_{20}N_2O_4S_2$	276–278[g]	>250[a,e]	...	..	...	...	...	..	...	...
CH_3S–R (III)	$C_{10}H_{13}NO_2S$	245–247[g]	10,000[b,d]	56.87	6.16	6.63	15.16	57.06	6.13	6.62	15.16
C_2H_5S–R (IV)	$C_{11}H_{15}NO_2S$	224–226[g]	3,000[c,d]	58.67	6.67	6.22	14.22	58.47	6.53	6.38	13.97
$CH_3S(=O)$–R (V)	$C_{10}H_{13}NO_3S$	250–251[h]	>10,000[e]	52.86	5.73	6.17	14.10	52.57	5.81	6.12	13.85
$CH_3S(=O)_2$–R (VI)	$C_{10}H_{13}NO_4S$	266–267[g]	>10,000[e]	49.39	5.36	5.64	12.90	48.92	5.84	5.52	12.86
NH_2SO_2–R (VII)	$C_9H_{12}N_2O_4S$	251–252[i]	>10,000[e]	44.30	4.93	11.47	13.11	44.06	4.84	11.31	13.21

[a] Insoluble at higher concentrations. [b] Inhibition was reversed by 50 γ of tyrosine, not by phenylalanine up to 1000 γ. [c] Inhibition was reversed by 100 γ of tyrosine, not by phenylalanine up to 1000 γ. [d] 500 γ reversed the inhibition of B-2-thienylalanine. [e] No effect on β-2-thienylalanine inhibition. [f] Recrystallized from 20% HCl. [g] Recrystallized from water. [h] Recrystallized from water–ethanol mixture. [i] Recrystallized from water–acetone mixture.

sulfonyl chloride with N-bromosuccinimide followed by selective reaction of the sulfonyl chloride group with ammonia. The resulting sulfamylbenzyl bromide was condensed with diethyl formamidomalonate and subsequently hydrolyzed and decarboxylated. This method gave a 27% yield of product based on the amount of *p*-toluenesulfonyl chloride consumed.

The compounds were assayed in the *E. coli* microbiological system described by Dittmer, *et al.*,[9] and the results are shown in Table II.

Acknowledgments.—The authors wish to express their appreciation to Mrs. G. M. Robinson who conducted the microbiological assays and to Dr. T. J. Bardos for helpful discussions and suggestions.

Experimental

Diethyl *p*-Xanthylbenzylacetamidomalonate (Ia).—To a stirred suspension of 16.15 g. (0.045 mole) of diethyl *p*-aminobenzylacetamidomalonate·HCl[2] in 30 ml. of 6 *N* HCl at 0° was added slowly 4.1 g. (0.06 mole) of sodium nitrite in 8 ml. of water. After the addition was completed, the solution was adjusted to *p*H 7 by the addition of solid sodium carbonate. The temperature was maintained at 0°, and a solution of 9.3 g. (0.058 mole) of potassium ethyl xanthate was added slowly. The solution was allowed to reach room temperature and then stirred at 60° for 1 hr. The product was extracted from the aqueous layer with three 100-ml. portions of ether. The ether solution was dried over magnesium sulfate and the ether distilled, leaving a viscous oil. The product was obtained by crystallization from 70% ethanol; yield 8.5 g. (47%), m.p. 103–105°.

p-Mercaptophenylalanine Hydrochloride (Thiotyrosine) (I).—A mixture of 1.0 g. (0.0028 mole) of Ia and 10 ml. of concentrated hydrochloric acid was refluxed for 5 hr. This solution was evaporated to 5 ml. under reduced pressure and chilled overnight. The product was collected and dried under vacuum over solid sodium hydroxide; yield 0.52 g. (86%), m.p. 243–246° dec. Recrystallization from 20% hydrochloric acid raised the melting point to 248–249° dec.[6]

p,p'-Phenylalanine Disulfide (II).—A solution of 0.3 g. (0.0015 mole) of I in 10 ml. of water was treated with a slight excess of 2 *N* iodine in 5% potassium iodide. This solution was heated on the steam-bath and adjusted to *p*H 5 with ammonium hydroxide. The white solid that precipitated upon cooling was collected and dried under vacuum; yield 0.16 g. (66%), m.p. 276–278° dec.[5]

Diethyl *p*-Methylmercaptobenzylacetamidomalonate (IIIa).—To a solution containing 7.4 g. (0.32 gram atom) of sodium dissolved in 700 ml. of absolute ethanol was added 69.9 g. (0.32 mole) of diethyl acetamidomalonate. Fifty-five grams (0.32 mole) of *p*-methylmercaptobenzyl

(9) K. Dittmer, G. Ellis, H. McKennis and V. du Vigneaud, *J. Biol. Chem.*, **164**, 761 (1946).

chloride[10] was added and the mixture refluxed for 2.5 hr. Approximately 80% of the alcohol was removed by distillation and 750 ml. of water was added. The crude product was collected by filtration and crystallized from 95% ethanol; yield 113 g. (84%). A sample was recrystallized from 95% ethanol for analysis, m.p. 108.5–109.5°.

p-**Methylmercaptophenylalanine (III).**—The amino acid was obtained by refluxing 5.0 g. (0.0136 mole) of IIIa with 50 ml. of concentrated hydrochloric acid for 4 hr. Upon cooling, the hydrochloride salt separated and was removed by filtration. It was dissolved in 100 ml. of hot water and neutralized to *p*H 7 with concentrated ammonium hydroxide. The amino acid which crystallized upon cooling was collected by filtration, washed with acetone and dried; yield 2.87 g. (95%), m.p. 245–247° dec.

Thioanethole (IVa).—To 120 ml. of cold 20% sodium hydroxide was added 50 g. (0.455 mole) of thiophenol. The mixture was stirred and 71 g. (0.46 mole) of diethyl sulfate was added dropwise over a period of 30 minutes. Stirring was continued for 4 hr. at room temperature and then the solution was extracted with ether. The ether extract was dried over magnesium sulfate and the ether removed by distillation. The residue was distilled under reduced pressure and the thioanethole collected at 89° (15 mm.); yield 52.6 g. (83%).

p-**Ethylmercaptobenzyl Chloride (IVb).**—A mixture of 45 g. (0.32 mole) of IVa, 26 g. (0.32 mole) of chloromethyl ether and 260 ml. of glacial acetic acid was heated at 65–70° for 40 hr. The solution was cooled, poured into 500 ml. of ice-water and extracted with chloroform. The chloroform extract was dried over magnesium sulfate and the chloroform removed by distillation. The residue was distilled under reduced pressure and the *p*-ethylmercaptobenzyl chloride collected at 149° (15 mm.), yield 20.3 g. (34%).

Anal. Calcd. for $C_9H_{11}ClS$: C, 57.92; H, 5.90; S, 17.17; Cl, 19.04. Found: C, 57.82; H, 5.82; S, 17.02; Cl, 19.13.

Diethyl *p*-**Ethylmercaptobenzylacetamidomalonate (IVc).** To a solution containing 1.93 g. (0.084 gram atom) of sodium dissolved in 210 ml. of absolute ethanol was added 18.2 g. (0.084) of diethyl acetamidomalonate. To this solution was added 15.6 g. (0.084 mole) of IVb and the mixture refluxed for 2 hr. Approximately 80% of the ethanol was removed by distillation and 400 ml. of water was added. The mixture was cooled and the crude product removed by filtration. Recrystallization from methanol–water yielded 19.7 g. (64%). A sample was recrystallized from 95% ethanol for analysis, m.p. 96–97°.

p-**Ethylmercaptophenylalanine (IV).**—The amino acid was obtained by refluxing 19 g. (0.0517 mole) of IVc with 190 ml. of concentrated hydrochloric acid for 4 hr. The hydrochloride salt crystallized on cooling and was collected by filtration. The salt was dissolved in 100 ml. of boiling water and adjusted to *p*H 7 by the addition of concentrated ammonium hydroxide. The amino acid crystallized on cooling and was collected by filtration; yield 7 g. (60%), m.p. 224–226° dec.

Diethyl *p*-**Methylsulfinylbenzylacetamidomalonate (Va).** To a solution of 11 g. (0.03 mole) of IIIa in 20 ml. of acetic acid was added 3.1 ml. (0.03 mole) of 30% hydrogen peroxide. The solution was cooled under tap water for a few minutes, stirred at room temperature for 15 minutes and then at 90° for 15 minutes. After cooling, the solution was poured into 150 ml. of water and cooled in the refrigerator. The crude product was collected by filtration and dried *in vacuo;* yield 8.2 g. (90%), m.p. 141–143°. A sample was recrystallized from water for analysis, m.p. 142–143°.

p-**Methylsulfinylphenylalanine (V).**—The amino acid was obtained by refluxing 22 g. (0.06 mole) of Va with 220 ml. of concentrated hydrochloric acid for 4 hr. The solution was evaporated to dryness under reduced pressure and the solid dissolved in 100 ml. of water. The free amino acid was obtained by passing the solution of hydrochloride salt through a column of Duolite A-2 ion-exchange resin. The resulting solution was evaporated to 50 ml. under reduced pressure, diluted with 50 ml. of ethanol and then chilled in an ice–salt bath. The product was collected by filtration and dried *in vacuo;* yield 7.5 g. (55%), m.p. 246–250° dec. A sample was recrystallized from water–ethanol for analysis, m.p. 250–251° dec.

Diethyl *p*-**Methylsulfonylbenzylacetamidomalonate (VIa).**—A mixture of 10.6 g. (0.03 mole) of IIIa, 9 ml. (0.08 mole) of 30% hydrogen peroxide and 30 ml. of acetic acid was heated on the steam-bath for 1 hr. An additional 3 ml. of 30% hydrogen peroxide was added and the heating continued for 30 minutes. Ten ml. of water was added to the hot solution and then it was cooled in the refrigerator. The crude product was collected by filtration and recrystallized from 95% ethanol; yield 8.2 g. (71%), m.p. 174–176°.

p-**Methylsulfonylphenylalanine (VI).**—The amino acid was obtained by refluxing 8.0 g. (0.021 mole) of VIa with 80 ml. of concentrated hydrochloric acid for 4 hr. The solution was evaporated to dryness under reduced pressure and the remaining solid was dissolved in 200 ml. of water. The solution was heated to boiling and adjusted to *p*H 7 by the addition of concentrated ammonium hydroxide. After cooling, the product crystallized and was collected by filtration; yield 4.3 g. (85%), m.p. 264–267° dec. A sample was recrystallized from water for analysis, m.p. 266–267° dec.

p-**Sulfamylphenylalanine (VII). Method A. Diethyl** *p*-**Chlorosulfonylbenzylacetamidomalonate (VIIa).**—A 150-ml. portion of chlorosulfonic acid was stirred at 15° and to it was added slowly 103 g. (0.335 mole) of diethyl benzylacetamidomalonate[11] over a period of 1 hr. The mixture was stirred 1 hr. at room temperature, 1 hr. at 65° and then allowed to stand overnight at room temperature. The mixture was added slowly to 750 g. of crushed ice. The crude product precipitated as a viscous oil. It was washed twice with cold water and finally with cold water containing 2% ether. The product was placed in a desiccator over calcium chloride and dried *in vacuo*. It was recrystallized from anhydrous chloroform–hexane to yield 65 g. (54%), m.p. 123–124°.

Anal. Calcd. for $C_{16}H_{20}ClNO_7$: C, 47.35; H, 4.93; N, 3.45; S, 7.89; Cl, 8.75. Found: C, 47.38; H, 4.91; N, 3.86; S, 7.89; Cl, 8.37.

Diethyl *p*-**Sulfamylbenzylacetamidomalonate (VIIb).**—A large excess of anhydrous ammonia was passed into a solution of 28 g. (0.069 mole) of VIIa in 200 ml. of anhydrous ether. The solid which was formed was collected by filtration, washed with ether and recrystallized from methanol–water to yield 14.2 g. (53%), m.p. 240–241°.

p-**Sulfamylphenylalanine (VII).**—The amino acid hydrobromide was obtained by refluxing 3 g. (0.008 mole) of VIIb with 20 ml. of 20% hydrobromic acid for 4 hr. The free amino acid was obtained by passing the solution of hydrobromide salt through a column of Duolite A-2 ion-exchange resin. The resulting solution was evaporated to 10 ml. under reduced pressure, and 10 ml. of acetone was added. The crude product was collected by filtration and recrystallized from water–acetone, m.p. 251–252° dec., yield 1.2 g. (63%).

p-**Sulfamylphenylalanine (VII). Method B.** α-**Bromo-***p*-**toluenesulfonyl Chloride (VIIc).**—A mixture of 49 g. (0.252 mole) of N-bromosuccinimide, 48 g. (0.252 mole) of *p*-toluenesulfonyl chloride and 2.42 g. (0.01 mole) of benzoyl peroxide in 250 ml. of carbon tetrachloride was refluxed for 2 hr. The mixture was cooled to room temperature and the succinimide removed by filtration. The carbon tetrachloride was removed from the filtrate by distillation under reduced pressure, and the oil that remained was extracted with three 150-ml. portions of boiling heptane. Fifty-five grams of crude product was obtained from the cooled extract. It was recrystallized from heptane to yield 51.3 g. (76%), m.p. 74–76°.

α-**Bromo-***p*-**toluenesulfonamide (VIId).**—A large excess of anhydrous ammonia was passed into a solution of 10 g. (0.037 mole) of VIIc in 350 ml. of anhydrous ether. The resulting precipitate was removed by filtration, washed with ether and crystallized from acetone, yield 7 g. (73%). A sample recrystallized from methanol–water for analysis, m.p. 191–192°.

Anal. Calcd. for $C_7H_8BrNO_2S$: C, 33.60; H, 3.24; N, 5.60; S, 12.80; Br, 32.00. Found: C, 33.58; H, 3.75; N, 5.69; S, 12.61; Br, 31.60.

Diethyl *p*-**Sulfamylbenzylformamidomalonate (VIIe).**—To a solution containing 0.45 g. (0.0195 gram atom) of

(10) Ng. Ph. Buu-Hoi and Ng. Hoan, *J. Org. Chem.*, **17**, 350 (1952).

(11) N. F. Albertson and S. Archer, THIS JOURNAL, **67**, 308 (1945).

sodium dissolved in 10 ml. of absolute ethanol was added 3.98 g. (0.0195 mole) of diethyl formamidomalonate. To this solution was added 4.92 g. (0.0195 mole) of VIId in 15 ml. of ethanol. The mixture was refluxed for 5 hr. and then evaporated to dryness under reduced pressure. One hundred ml. of water was added with stirring, the solid removed by filtration and recrystallized from ethanol; yield 4.6 g. (63%), m.p. 236–240°. A sample was recrystallized from dioxane–heptane for analysis, m.p. 239–240°.

p-**Sulfamylphenylalanine (VII).**—The amino acid hydrochloride was obtained by refluxing 21 g. (0.056 mole) of VIIe with 200 ml. of concentrated hydrochloric acid for 5 hr. The solution was evaporated to dryness under reduced pressure. The hydrochloride salt was dissolved in 100 ml. of water and the solution passed through a column of Duolite A-2 ion-exchange resin to obtain the free amino acid. The resulting solution was evaporated to 125 ml. under reduced pressure and 100 ml. of acetone added. The solution was cooled overnight and the crude product was collected; yield 10.5 g. (76%), m.p. 248–249° dec. A sample was recrystallized from water–acetone for analysis, m.p. 251–252° dec.

KANKAKEE, ILLINOIS

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

Organic Sulfur Derivatives. II.[2] Sulfides, Sulfoxides and Sulfones from Thiols and 10-Undecenoic Acid

BY N. H. KOENIG AND DANIEL SWERN

RECEIVED FEBRUARY 22, 1957

Sulfides are formed by the addition of thiols (RSH) to 10-undecenoic acid (equation 1). The reactions proceed moderately rapidly at temperatures below 100° under free-radical conditions, often with the assistance of ultraviolet light. The acids [$RS(CH_2)_{10}CO_2H$] have a terminal substituent R, which is alkyl (propyl, butyl, hexyl, heptyl, octyl, undecyl or dodecyl), hydroxyethyl, carboxymethyl, acetyl, benzyl, phenyl or 2-naphthyl. Some of the sulfides have been oxidized to sulfoxides by bromate–bromide solution; many have been oxidized to sulfones by peracetic acid. However, an attempt to prepare the sulfone of 11-(acetylthio)-undecanoic acid yielded 11-sulfoundecanoic acid. Other compounds prepared include diesters of 11-(carboxymethylthio)-undecanoic acid and a sulfonium salt, methyl-*n*-octyl-10-carboxydecylsulfonium iodide.

This investigation continues our systematic study of the preparation of long-chain sulfur compounds of known structure. In our first paper[2] it was shown that a high yield of 11-(carboxymethylthio)-undecanoic acid readily is obtained by the addition of an equimolar amount of mercaptoacetic acid to 10-undecenoic acid. We have now shown that this reaction is general. It has been extended to include many other thiols; the resulting (alkylthio)- and (arylthio)-undecanoic acids have been converted in many instances to sulfoxides, sulfones, esters and other derivatives. Aside from 11-(carboxymethylthio)-undecanoic acid,[3] 11-(*n*-dodecylthio)-undecanoic acid[3] and 11-sulfoundecanoic acid,[4] all of the compounds described in this paper are new. Some similar alkylthio, alkylsulfinyl and alkylsulfonyl acids, prepared in different ways, have been reported.[5,6]

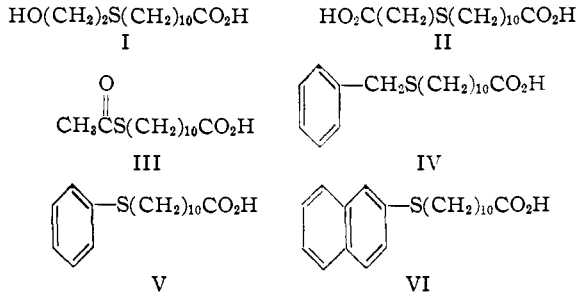
Alkanethiols add moderately rapidly to 10-undecenoic acid as shown in equation 1. Previous evidence,[2] as well as infrared and X-ray diffraction studies to be reported separately, indicates that

$$RSH + CH_2{=}CH(CH_2)_3CO_2H \longrightarrow RS(CH_2)_{10}CO_2H \quad (1)$$

R = *n*-propyl, butyl, hexyl, heptyl, octyl, undecyl or dodecyl.

the addition products isolated have an unbranched structure, *i.e.*, the sulfur atom is attached at the 11-(terminal) rather than at the 10-position, and that they are formed *via* free-radical intermediates. The free-radical addition mechanism is also supported by the activating influence of ultraviolet light.

Other types of terminally substituted undecanoic acids, (I-VI) are formed by the addition of mercaptoethanol, mercaptoacetic acid, thiolacetic acid, α-toluenethiol, benzenethiol or 2-naphthalenethiol, respectively.



The pure acids, $RS(CH_2)_{10}CO_2H$, are odorless, white, crystalline solids. They are insoluble in water, sparingly soluble in petroleum ether at room temperature or 0° and moderately soluble in more polar solvents such as acetone and ethanol. Other characteristics of these compounds are given in Table I.

The chemical behavior of these sulfides is illustrated by some reactions of 11-(*n*-octylthio)-undecanoic acid, $CH_3(CH_2)_7S(CH_2)_{10}CO_2H$ (VII). Controlled oxidation with bromate–bromide solution gives the sulfoxide VIII, while excess peracetic acid forms the sulfone IX. Methyl iodide adds to

$$CH_3(CH_2)_7SO_x(CH_2)_{10}CO_2H \quad \text{VIII, } x = 1 \quad \text{IX, } x = 2$$

VII to give the sulfonium salt, methyl-*n*-octyl-10-carboxydecylsulfonium iodide (X). The carboxyl

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(2) Paper I, N. H. Koenig and D. Swern, THIS JOURNAL, **79**, 362 (1957).

(3) G. E. Serniuk, F. W. Banes and M. W. Swaney, *ibid.*, **70**, 1804 (1948).

(4) W. Rigby, *J. Chem. Soc.*, 2560 (1956).

(5) L. Rapoport, A. Smith and M. S. Newman, THIS JOURNAL, **69**, 893 (1947).

(6) B. Smith and S. Hernestam, *Acta Chem. Scand.*, **8**, 1111 (1954).