acidic to benzopurpurin paper. The solid present was collected, washed with water, dried, and recrystallized from 80 ml. of 2-ethoxyethanol to give 18.5 g. (27% recovery) of yellow needles, m.p. 147–148°. A mixture melting point determination with starting material showed no depression (148–149°).

2-Diphenylacetyl-2-piperidino-1,3-indandione. To a solution at 20° of 29.7 g. (0.071 mole) of 2-bromo-2-diphenylacetyl-1,3-indandione (III) in 1200 ml. of dioxane was added gradually with swirling 21.0 ml. (18.1 g., 0.213 mole) of piperidine. The mixture warmed spontaneously to 43°. After standing overnight the piperidinium bromide which had separated was removed by filtration and washed with dioxane and acetone; 5.5 g. (47%), m.p. and mixture m.p. 240–241°. The bright orange mother liquor and the dioxane wash were combined, evaporated under reduced pressure, and the dark, viscous residue allowed to crystallize at 5° from 140 ml. of carbon tetrachloride. The solid which separated, after washing with carbon tetrachloride and water, amounted to 11.6 g., m.p. 181–187 . Recrystallization from methyl ethyl ketone gave 6.6 g. (22%) of bright yellow rods, m.p. 192–193°.

Anal. Calcd. for $C_{28}H_{25}O_3N$: C, 79.41; H, 5.95; N, 3.31. Found: C, 79.8; H, 6.12; N, 3.35.

Acknowledgments. The interest and helpful suggestions of Drs. P. F. Dreisbach, J. J. Denton, and R. P. Parker are acknowledged with appreciation. Thanks are given to Mr. O. E. Sundberg, Miss Irene Prokul, and Mr. David Green for the microanalyses and to Mrs. Cecelia Jorgensen for the infrared spectral analyses and their interpretation.

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Decarboxylation of Thetin Salts

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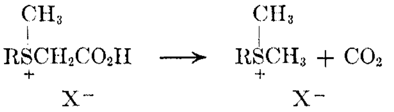
Dialkyl thetin salts, $R_1R_2\overset{+}{S}CH_2CO_2H{\cdot}X^-$, undergo facile decarboxylation to the corresponding trialkylsulfonium salts. The presence of an electron-donating (methyl) group on the alpha-carbon tends to suppress the reaction.

To the ever-increasing accounts of differences in reactivity,[1] conjugative ability[2,3] and the like between numerous sulfonium and ammonium compounds should be added another example of considerable interest. In the course of a study of various long-chain thetin salts (I), it was discovered that facile decarboxylation occurrred under relatively mild conditions to give the corresponding trialkyl sulfonium salts.



$$R\underset{+}{\overset{CH_3}{S}}CH_2CO_2H\ X^- \longrightarrow R\underset{+}{\overset{CH_3}{S}}CH_3\ X^- + CO_2$$

I

This reaction is virtually unknown in the corresponding betaine (ammonium) series, in which the compounds are ordinarily stable at temperatures below their melting points which often run in excess of 200°. A noteworthy exception[4] has been reported with the betaine derived from 2,5-dimethylpyrazine, in which case decarboxylation is facilitated by an intermediate capable of resonance stabilization.

The reaction was first encountered in alkaline hydrolysis of carbethoxymethyl(dodecyl)methylsulfonium *p*-toluenesulfonate. The identity of the product as dodecyldimethylsulfonium *p*-toluenesulfonate was shown by (1) analysis, (2) the infrared spectrum which indicated the absence of carboxyl ion and the presence of *p*-toluene–sulfonate ion, and (3) comparison with an authentic specimen. Dodecylmethylthetin, the expected product, was prepared by the action of silver oxide on the thetin hydrochloride and proved to be quite stable in contrast to the report of Werntz,[5] who used alkali to liberate this thetin from its salt. The thetin can also be reconverted to a salt, as shown by the reaction of dodecylmethylthetin with *p*-toluenesulfonic acid. The decarboxylation of the thetin salts is quite general, as was later confirmed in the cases of the decyl, tetradecyl, hexadecyl, and decamethylenebis analogs.

The ease with which decarboxylation of dodecyldimethylthetin *p*-toluenesulfonate occurs was shown by experiments carried out in refluxing acetone. At this relatively low temperature (56°), decarboxylation occurred readily and was complete within 2 hours in the presence of such mildly basic catalysts as piperidine, Amberlite IR-4B, and dodecylmethylthetin, itself. In the absence of a catalyst, no reaction was apparent after 1 hour, but, after 6 hours, a 94% yield of decarboxylated product was obtained. Evidently the reaction is extremely slow at first, until a sufficient quantity

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(1) W. E. Doering and K. Schreiber, *J. Am. Chem. Soc.*, **77**, 514 (1955).

(2) F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **78**, 87 (1956).

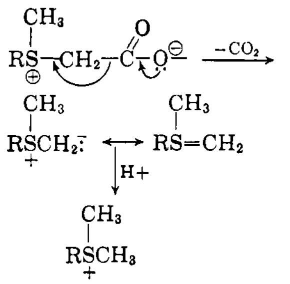
(3) N. F. Blau and C. G. Stuckwisch, *J. Org. Chem.*, 22, 82 (1957).

(4) E. V. Hort and P. E. Spoerri, *J. Am. Chem. Soc.*, **77**, 5898 (1955).

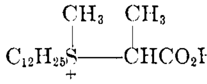
(5) J. H. Werntz, U. S. Patent **2,178,353**, October 31, 1939; *Chem. Abstr.*, **34**, 1419 (1940).

of the dodecyldimethylsulfonium *p*-toluenesulfonate[6] is formed to act as a catalyst. Acetic acid, however, did not completely inhibit the reaction, for, after 2 hours, decarboxylation was about one-third complete.

The ease with which thetin salts undergo decarboxylation may well be attributed to resonance forms arising from an expansion of the valence shell of the sulfur atom, a phenomenon which is essentially impossible with nitrogen; accordingly, the following course of reaction is proposed:



The effect of substitution at the alpha-carbon atom by the methyl group was investigated briefly with the expected result. Decarboxylation was rendered exceedingly more difficult; an acetone solution of dodecylmethyl-α-propiothetin *p*-toluenesulfate (II) required prolonged refluxing (6 hours) in the presence of a piperidine catalyst to effect complete reaction. The reaction proceeded readily, however, at temperatures above the fusion point of the pure substance (*ca.* 160°). It is apparent that the inductive effect of the sulfonium group is partially satisfied by the electron-donating α-methyl group.



$$C_{12}H_{25}\overset{CH_3}{\underset{+}{S}}—\overset{CH_3}{C}HCO_2HC_7H_7SO_3^-$$

II

Previous evidence relating to the decarboxylation of thetin salts appears to be limited to that of Weibull,[7] who detected cyclohexyldimethylsulfonium and carbonate ions among numerous products of decomposition of cyclohexylmethylthetin hydrobromide under the influence of alcoholic potassium hydroxide.

EXPERIMENTAL[8]

Although specific examples are given in the following paragraphs, most of the procedures are quite generally applicable to the other members of the homologous series with minor modifications. Properties and yields of the various compounds prepared are to be found in Tables I–IV.

TABLE I

Ethyl *n*-Alkylmercaptoacetates ($RSCH_2CO_2C_2H_5$)

R	B.P., °C./Mm. or M.P.	n_D^{25}	Yield, %
C_7H_{15}	120–123/9	—	81
C_9H_{19}	101–105/0.25–0.35	1.4585	65
$C_{10}H_{21}$	117–119/0.7	1.4615	70+
$C_{12}H_{25}$	137–139/0.35	1.4604	76
$C_{14}H_{29}$	133–143/0.3	1.4629	83
$C_{16}H_{33}$	166–168/0.35	1.4640	82
$—(CH_2)_{10}—$	187–215/0.30–0.37	1.4902	81

TABLE II

n-Alkyl Methyl Sulfides
($RSCH_3$ and $CH_3S(CH_2)_nSCH_3$)

R	B.P., °C./Mm. or M.P.	n_D^{25}	Yield, %
$C_{10}H_{21}$	118–119/11[a]	1.4567	86
$C_{12}H_{25}$	156–159/17[b]	1.4582	87
$C_{14}H_{29}$	134–140/0.35–0.5[c]	1.4594	88
$C_{16}H_{32}$	134–156/0.33–0.37[b]	1.4615	81
$—(CH_2)_2—$	181–183[d]	1.5260	74
$—(CH_2)_5—$	127/10[d]	1.5065	49[e]
$—(CH_2)_{10}—$	117–131/0.4[f]	1.4938	72

[a] J. von Braun, W. Teuffert, and K. Weissbach, *Ann.*, **472,** 139 (1929), report b.p. 125° (13 mm.) [b] R. Kuhn and O. Dann, *Ber.*, **73B,** 1092 (1940), report b.p. 163–165° (19 mm.) for dodecyl and m.p. 19.5–20.5° for hexadecyl compound. [c] *Anal.* Calcd. for $C_{15}H_{32}S$: C, 73.8; H, 13.1. Found: C, 74.0; H, 13.4. [d] M. Protiva, J. O. Jilek, and O. Exner, *Chem. Listy*, **47,** 580 (1953); [*Chem. Abstr.*, **49,** 155 (1955)] report b.p. 78–80° (10–12 mm.) for C_2 and b.p. 112–114° (8 mm.) for C_5 compound. [e] Low owing to accidental loss. [f] D. Jerchel, L. Dippelhoffer, and D. Renner, *Chem. Ber.*, **87,** 947 (1954), report b.p. 206° (19 mm.).

I. *Ethyl hexadecylmercaptoacetate.* To a solution of 6.9 g. (0.3 g. atom) of sodium in 150 ml. of methanol was added 36 g. (0.3 mole) of ethyl mercaptoacetate, followed by 91.5 g. (0.3 mole) of 1-bromohexadecane. The solution was heated at reflux for 2 hr., cooled, and 150 ml. of water added. The product was extracted with ether, dried, and distilled through a 10-inch heated column packed with Berl Saddles, using a variable reflux head. Yield, 84 g. (82%); b.p. 166–168° (0.35 mm.); n_D^{25} 1.4640.

II. *Hexadecylmercaptoacetic acid.* A. *From the ester.* Hydrolysis of the ester in a 10% ethanol solution yielded 96% of the acid as colorless plates; m.p. 75–76° (from hexane).[9]

B. *By a Williamson synthesis.*[10] The acid was also prepared directly from 1-bromohexadecane and mercaptoacetic acid as in Section I, but using two equivalents of sodium. After the addition of water to the reaction mixture, it was heated until solution was complete, and was acidified with excess hydrochloric acid. Recrystallization of the crude product from methanol yielded 86% of the acid; m.p. 74.5–75.5°.

III. *α-Dodecylmercaptopropionic acid.* To a cooled solution of 11.5 g. (0.5 mole) of sodium in 400 ml. of methanol was added 50.5 g. (0.25 mole) of *n*-dodecanethiol, followed by 38.2 g. (0.25 mole) of α-bromopropionic acid. The solution was stirred and cooled in an ice bath during the addition and

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(6) A 1% acetone solution of the sulfonium salt gave a reading of 7.65 at 40° on a Beckman *p*H meter.

(7) B. Weibull, *Arkiv Kemi*, **3,** 171 (1951); *Chem. Abstr.*, **46,** 3962 (1952).

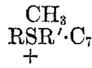
(8) All melting points obtained by capillary method and corrected.

(9) A. J. Hill and E. W. Fager, *J. Am. Chem. Soc.*, **65,** 2300 (1943), report 73.5–74° for m.p.

(10) By this procedure the decyl compound, m.p. 51–52°, and dodecyl compound, m.p. 61.5–62.5°, were prepared in 64 and 82% respective yields. L. Rapoport, A. Smith, and M. S. Newman, *J. Am. Chem. Soc.*, **69,** 693 (1947), report 52–53° and 61–62° for the melting points of decyl and dodecylmercaptoacetic acids.

TABLE III

SULFONIUM *p*-TOLUENESULFONATES



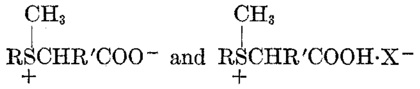
$$\overset{CH_3}{\underset{+}{RSR'}}\cdot C_7H_7SO_3^-$$

R	R′	Method Used	M.P., °C.	Yield, %	Analyses Calcd. C	Calcd. H	Calcd. S	Found C	Found H	Found S	Formula
C_7H_{15}	$CH_2CO_2C_2H_5$	VA	[a]	84							
C_9H_{19}	$CH_2CO_2C_2H_5$	VA	75–76.5[a]	81							
$C_{10}H_{21}$	$CH_2CO_2C_2H_5$	VA	77–81[a]	90							
$C_{12}H_{25}$	$CH_2CO_2C_2H_5$	VA	92–94[b]	68	60.7	8.9	13.5	60.5	8.9	13.8	$C_{24}H_{42}O_5S_2$
$C_{14}H_{29}$	$CH_2CO_2C_2H_5$	VA	82–86[a]	74							
$C_{16}H_{33}$	$CH_2CO_2C_2H_5$	VA	87–90[a]	78							
$-(CH_2)_{10}-$	$CH_2CO_2C_2H_5$	VA	55–59[a]	77							
C_7H_{15}	CH_3	VB	183.5–185	62	57.8	8.4	19.25	57.8	8.4	19.6	$C_{16}H_{28}O_3S_2$
C_9H_{19}	CH_3	VB	179–181.5	68	60.0	8.9	17.8	60.0	8.9	17.9	$C_{18}H_{32}O_3S_2$
$C_{10}H_{21}$	CH_3	VA and B	169.5	79	60.9	9.2	17.1	61.0	9.1	16.7	$C_{19}H_{34}O_3S_2$
$C_{12}H_{25}$	CH_3	VA and B	164–170	74	62.8	9.5	15.9	62.8	9.3	15.6	$C_{21}H_{38}O_3S_2$
$C_{14}H_{29}$	CH_3	VA and B	163.5–180.5	71	64.2	9.8	14.9	64.4	9.9	15.2	$C_{23}H_{42}O_3S_2$
$C_{16}H_{33}$	CH_3	VA and B	163.5–182.5	78	65.4	10.0	14.0	65.1	10.3	14.3	$C_{25}H_{46}O_3S_2$
$-(CH_2)_5-$	CH_3	VA	129–130	50	51.5	6.7	23.9	51.6	6.7	24.2	$C_{23}H_{36}O_6S_4$
$-(CH_2)_{10}-$	CH_3	VA and B	182–183	92	55.4	7.6	21.1	55.4	7.7	20.9	$C_{38}H_{46}O_6S_4$

[a] Not purified. [b] Crude product melted at 66–80°; purified by repeated recrystallization from acetone.

TABLE IV

THETINS AND THEIR SALTS



$$R\overset{CH_3}{\underset{+}{S}}CHR'COO^- \text{ and } R\overset{CH_3}{\underset{+}{S}}CHR'COOH\cdot X^-$$

R	R′	X⁻	Method Used	M.P., °C.	Yield, %	Analyses Calcd. C	Calcd. H	Calcd. S	Found C	Found H	Found S	Formula
$C_{10}H_{21}$	H	$C_7H_7SO_3^-$	VA	107–135 (dec.)	50	57.4	8.2	15.3	57.6	8.5	15.1	$C_{20}H_{34}O_5S_2$
$C_{12}H_{25}$	H	—	VIB	102–108 (dec.)	62	65.7	11.0	11.7	65.9	10.9	11.4	$C_{15}H_{30}O_2S$
$C_{12}H_{25}$	H	Cl^-	VIA	68–100	41	57.9	10.0	10.3	57.6	10.3	10.5	$C_{15}H_{31}ClO_2S$
$C_{12}H_{25}$	H	$C_7H_7SO_3^-$	VA and VIC	114–135 (dec.)	73	59.2	8.6	14.4	59.1	8.4	14.2	$C_{22}H_{38}O_5S_2$
$C_{12}H_{25}$	CH_3	$C_7H_7SO_3^-$	VA	154–155 (dec.)	55	60.0	8.7	13.9	60.3	8.9	13.7	$C_{23}H_{40}O_5S_2$
$C_{16}H_{33}$	H	$C_7H_7SO_3^-$	VA	121.5–141 (dec.)	65	62.2	9.2	12.75	62.5	9.5	12.7	$C_{26}H_{46}O_5S_2$

allowed to warm up gradually to 25°. After 2 hr. at reflux, one half of the methanol was removed and 110 ml. of 10% hydrochloric acid added. The product which separated was isolated and recrystallized from hexane; yield 50.4 g. (74%); m.p. 51–52°.

Anal. Calcd. for $C_{15}H_{30}O_2S$: C, 65.75; H, 10.95. Found: C, 65.9; H, 11.2.

IV. *Dodecyl methyl sulfide.* This was prepared by essentially the same procedure as in I with added precautions. The low-boiling methyl mercaptan (b.p. 6°) was chilled in an ice-salt bath and added to an ice cold solution of sodium methoxide. After addition of the alkyl bromide, the solution was heated *carefully* to the reflux temperature. An exothermic reaction soon occurred, necessitating immediate cooling to avoid loss. Thereafter, the reaction and workup proceeded normally.

V. *Dodecyldimethylsulfonium p-toluenesulfonate.* A. *Direct synthesis.* A mixture of 216 g. of dodecyl methyl sulfide and 475 g. (a 7% excess) of freshly distilled methyl *p*-toluenesulfonate was heated on a steam-bath for 3 hr.; benzene was added as necessary to control frothing. When cool, the product was filtered, washed with benzene, and recrystallized from 1 l. of absolute ethanol, using Nuchar, and again from 800 ml. of fresh solvent, giving 530 g. of colorless plates; m.p. 164–170°. Concentration of the ethanolic filtrates produced a large second crop (172 g.) of slightly less pure material. Total yield, 702 g. (74%).

B. *From carbethoxymethyl(dodecyl)methylsulfonium p-toluenesulfonate.* A solution of 439 g. (0.93 mole) of the ester-salt (prepared as in A preceding paragraph from ethyl dodecylmercaptoacetate) in 650 ml. of 95% ethanol containing 61.2 g. of potassium hydroxide (85% pellets) was heated at reflux for 2.5 hr. and filtered hot. The filtrate was concentrated to 400 ml. and 4 l. of ether added. The crude, white crystalline product was isolated and extracted with 18 l. of boiling acetone, the undissolved potassium *p*-toluenesulfonate being filtered off. The filtrate was concentrated to one-half volume and cooled, to give 211 g. (57%) of large, colorless plates; m.p. 163–170°.

Further consecutive recrystallizations from acetonitrile, absolute ethanol, and acetone failed to change the melting point of this compound.

C. *From dodecylmethylthetin p-toluenesulfonate.* See Section VII.

VI. *Dodecylmethylthetin (DMT).* A. *DMT hydrochloride.* A mixture of 64.8 g. (0.3 mole) of dodecyl methyl sulfide and 28.5 g. (0.3 mole) of chloroacetic acid was heated, with stirring, at 60–65° for 1 hr. and allowed to stand overnight. Dry ether (800 ml.) was added, but the white, crystalline solid was too sticky to filter. The ether was removed, and 1 l. of benzene was distilled from the residue, using a 55° bath. This residue, after 3 hr. at 20 mm., was allowed to stand for several days until more than half the mass had crystallized. Dilution with 800 ml. of dry ether gave 40.4 g. (41%) of crude product, m.p. 65–98°, which, after recrystallization from 140 ml. of acetone, amounted to 21.5 g.; m.p. 68–100°. Further recrystallization failed to improve the melting point.

B. *DMT.* To a solution of 6.0 g. of DMT hydrochloride in 50 ml. of dry methanol was added 2.7 g. (20% excess) of silver oxide, and the mixture was shaken for 1.5 hr. After filtration through Super Filtrol and removal of the solvent (bath <40°), the white, crystalline residue was redissolved in 4 ml. of dry methanol and reprecipitated by addition of 50 ml. of dry ether; yield, 3.3 g. (62%); m.p. 101–109° (dec.); Beilstein test, negative. Recrystallization from methanol-ether, ether being added only up to the point of crystallization, produced m.p. 102–108° dec.).

C. *Dodecylmethylthetin p-toluenesulfonate.* Although for preparative purposes the method of Section VA would be used, the following is of interest.

An equimolar mixture of dodecylmethylthetin and p-toluenesulfonic acid was heated in acetone for 1.25 hr. Cooling produced silky needles of dodecylmethylthetin p-toluenesulfonate in 56% yield; m.p. 113–133° (dec.), not depressed by a sample prepared by the aforementioned method.

VII. *Decarboxylation of DMT p-toluenesulfonate.* An example has already been given (Section VB) where decarboxylation occurred during the course of the reaction. Other examples are outlined in succeeding sections.

A. *With Amberlite IR-4B.* A 4-g. sample of DMT p-toluenesulfonate was heated in 750 ml. of refluxing acetone for 2 hr. in the presence of 24 g. of acetone-washed Amberlite IR-4B. Filtration and cooling produced 2.5 g. (70%) of dodecyldimethylsulfonium *p*-toluenesulfonate; m.p. 163–170°.

B. *With piperidine.* Reaction as in A, with one small drop of piperidine in place of the Amberlite resin and concentration of the reaction mixture, produced 3.5 g. (97%) of the decarboxylated product, m.p. 163–169°.

C. *With DMT.* Reaction of equivalent amounts of DMT and DMT *p*-toluenesulfonate under conditions of Section A produced a 60% yield of the decarboxylated product; m.p. 163–169.5°.

D. *With acetic acid.* Reaction as in A, with one drop of acetic acid in place of the Amberlite resin and concentration to one-fifth volume, gave a 62% recovery of impure starting material. A second crop consisted of 27% of dodecyldimethylsulfonium *p*-toluenesulfonate, m.p. 163.5–169.5°.

E. *No catalyst.* When DMT *p*-toluenesulfonate was heated for 1 hr. in refluxing acetone without a catalyst, no reaction was apparent and the starting material was recovered unchanged. However, after 6 hr., a 94% yield of the decarboxylated product, m.p. 163.5–169°, was obtained.

VIII. *Decarboxylation of dodecylmethyl-α-propiothetin p-toluenesulfonate* (II). A. *No catalyst.* A solution of 4.0 g. of the thetin salt in 1400 ml. of boiling acetone was sampled at intervals of 1, 5, and 7 hr. The crystals separating from the concentrated ($^1/_3$ vol.) sample melted 2.5°, 5.5°, and 6.5° lower, respectively, than the original pure salt, and mixtures with the latter were undepressed. The recovered crystalline material (3.5 g.) was shown by infrared analysis to consist almost exclusively of thetin salt (strong band at 1710 cm.$^{-1}$).

B. *With piperidine.* A solution of 2 g. of the salt in 750 ml. of boiling acetone containing 6 drops of piperidine was sampled after 3 hr.; a 5.5° drop in melting point had occurred. After 6 hr., crystallization did not readily occur. The solvent was evaporated and the residue washed with ether to give 1.55 g. of colorless crystals, m.p. 75–88°. The infrared curve, showing the complete absence of thetin salt, strongly resembled that of dodecyldimethylsulfonium *p*-toluenesulfonate.

C. *By heat.* The dry salt was warmed in a test tube at 160° until the evolution of carbon dioxide had ceased. The resulting oil was shown by infrared analysis to contain a substantial amount (20–30%) of non-decarboxylated thetin salt. Under the same conditions decarboxylation of dodecylmethylthetin *p*-toluenesulfonate is essentially complete.

Acknowledgment. The author is indebted to D. W. Stewart and Thelma J. Davis, of these Laboratories, for infrared analyses.

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