terial was purified by neutralization with aqueous sodium bicarbonate solution, dissolution of the free amine in ethyl alcohol, and subsequent reacidification with alcoholic hydrogen chloride. The purified material melted at 177–178° dec.

Anal. Calcd. for $C_{16}H_{22}N_2O_5Cl_2$: C, 48.86; H, 5.64; N, 7.13. Found: C, 49.10; H, 5.83; N, 7.08.

RAHWAY, N. J. RECEIVED JUNE 22, 1951

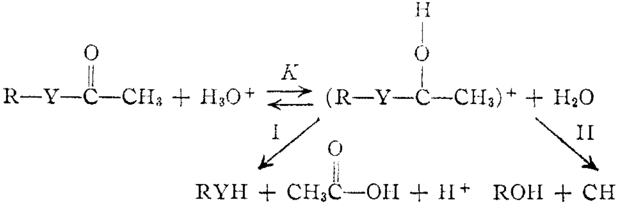
[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Cleavage of the Carbon–Sulfur Bond. Rates of the Basic and the Acid-catalyzed Hydrolysis of Allyl, Benzyl and Trityl Thioacetates, and the Corresponding Acetates in Aqueous Acetone Solution

BY BETSY K. MORSE AND D. STANLEY TARBELL

The kinetics of the acidic and basic hydrolysis of allyl, benzyl and trityl thiolacetates and the corresponding acetates have been determined in 62% aqueous acetone. The acid-catalyzed hydrolysis of trityl thiolacetate leads to alkyl–sulfur cleavage with the formation of triphenylcarbinol. The reaction is characterized by a large E and a positive $\Delta S^{\ddagger}$. In contrast to the rapid solvolysis of trityl acetate, the alkaline hydrolysis of trityl thiolacetate proceeds at a rate comparable to those of the other esters, and does not appear to involve alkyl–sulfur cleavage. The energy terms for the hydrolysis reactions are compared with those for alkyl acetates and thiolacetates which have been previously studied.

In the acid-catalyzed hydrolysis of ester and thiol esters, two types of fission are possible, either Y-acyl (I) or Y-alkyl (II).[1]



$$R{-}Y{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_3 + H_3O^+ \overset{K}{\rightleftarrows} (R{-}Y{-}\overset{\overset{\displaystyle H}{|}\atop\overset{\displaystyle O}{|}}{C}{-}CH_3)^+ + H_2O$$

$$\text{I}: \; RYH + CH_3\overset{\overset{\displaystyle O}{\|}}{C}{-}OH + H^+ \qquad \text{II}: \; ROH + CH_3\overset{\overset{\displaystyle O}{\|}}{C}{-}YH + H^+$$

The formation of the transition state intermediate for path I is visualized as a weakening of the acyl–Y bond upon the attack of water on the conjugate acid of the ester, accompanied by solvation of RY. By path II, solvation of the departing group, R^+, is required with the weakening of the alkyl–Y bond. The cleavage step (either I or II) is the rate-determining step; the reversible addition of the proton, defined by the equilibrium constant K, is rapid.[2]

It has been suggested[3] that *t*-butyl acetate hydrolyzes by alkyl–oxygen cleavage (path II), and this idea was supported by kinetic data given in the preceding paper of this series.[4] It was further shown[4] that *t*-butyl thiolacetate hydrolyzed by path I, a result which is not unexpected in view of the very numerous observations indicating that alkyl–sulfur cleavage occurs much more slowly than alkyl–oxygen cleavage.[5] However, esters of trityl mercaptan have been shown to undergo alkyl–sulfur cleavage[6] under strongly acidic conditions. The object of the present work was to measure rates of the acid-catalyzed and basic hydrolyses of some esters and thiolesters which might be expected to hydrolyze by path II.

Acid-catalyzed Hydrolysis.—It was found on qualitative experiments that trityl acetate, $(C_6H_5)_3COCOCH_3$, was hydrolyzed instantly even in neutral solution.[7] The sulfur analog, trityl thiolacetate, hydrolyzed at a measurable rate, with the formation of triphenylcarbinol, which was isolated and identified; thus alkyl–sulfur cleavage was indicated. Trityl mercaptan was stable under the conditions of the hydrolysis and therefore could not be a precursor of the triphenylcarbinol, according to the scheme

$$(C_6H_5)_3CSCOCH_3 + H_3O^+ \longrightarrow (C_6H_5)_3SH + CH_3COOH \xrightarrow{H_2O} (C_6H_5)_3COH + H_2S$$

The acid hydrolysis of benzyl thiolacetate was shown to proceed by path I, with the formation of benzyl mercaptan, by the isolation of the crystalline benzyl 3,5-dinitrothiolbenzoate, $(O_2N)_2C_6H_3COSCH_2C_6H_5$, from the hydrolysis product. A similar investigation of the hydrolysis product from allyl thiolacetate yielded insufficient low-boiling material for the conclusive identification of allyl mercaptan, but it appeared that oxidation or polymerization products of allyl mercaptan, were present, and hence that this hydrolysis likewise had proceeded by path I.

The details of the acid-catalyzed hydrolyses are given in Table I, where the pseudo first-order constants are given. In Table II are given the Arrhenius activation energies, E, and the other energy terms, obtained in the usual way.[8] The corresponding terms for the alkyl acetates and thiolacetates have been calculated from the data of Rylander and Tarbell[4] and are tabulated for comparison with the results of the present study. All of the quantities in this table are subject to the ambiguity previously mentioned.[2]

The most striking thing in Table II is that the

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(1) Day and Ingold, *Trans. Faraday Soc.*, **376**, 686 (1941).

(2) The pseudounimolecular rate-constants, in which rates of acid-catalyzed hydrolysis of esters are usually expressed, are composite constants, as is clear from the exact rate equation, $-d(\text{ester})/dt = kK(H_3O^+)(\text{ester})$, where k is the specific rate constant for path I or II, and K is the equilibrium constant defined above. The temperature coefficient of the observed rate constant thus includes an unknown contribution whose amount depends on the heat of reactions for the rapid reversible addition of the proton to the ester (*cf.* Carlin, Nelb and Odioso, THIS JOURNAL, **73**, 1006 (1951)).

(3) Cohen and Schneider, *ibid.*, **63**, 3382 (1941).

(4) Rylander and Tarbell, *ibid.*, **72**, 3021 (1950).

(5) Tarbell and Harnish, *Chem. Revs.*, **49**, 1 (1951).

(6) Iskander, *Nature*, **155**, 141 (1945).

(7) Gomberg and Davis (*Ber.*, **36**, 3926 (1903)) reported that trityl acetate is converted rapidly by water or alcohol to triphenylcarbinol or its ethyl ether. Hammond and Rudesill, THIS JOURNAL, **72**, 2769 (1950), have recently shown that trityl benzoate, in methyl ethyl ketone–alcohol solution, is converted to trityl ethyl ether by a first-order solvolysis, with alkyl–oxygen fission (path II).

(8) Glasstone, Laidler and Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941.

TABLE I

FIRST-ORDER RATE CONSTANTS FOR ACID-CATALYZED HYDROLYSIS OF $RSCOCH_3$ AND $ROCOCH_3$ IN 62% AQUEOUS ACETONE

R	Initial concn. m./l. × 10^2 Ester	Initial concn. m./l. × 10^2 HCl	Temp., °C.	$k \times 10^5$, sec.$^{-1}$
		Thiolacetates, $RSCOCH_3$		
Allyl	5.260	5.114	42.06	1.05 ± 0.04
	5.243	5.645	56.00	3.1 ± 0.2
	6.861	6.218	68.72	7.6 ± 0.1
Benzyl	4.684	5.057	40.04	0.44 ± 0.02
	7.180	6.950	56.00	2.01 ± 0.04
	7.180	6.950	68.72	5.62 ± 0.07
	4.684	5.057	68.72	6.60 ± 0.05
Trityl	0.308	1.099	40.04	12.7 ± 0.1
	.372	1.207	56.00	112 ± 5
	.372	1.207	68.72	630 ± 20
	.308	1.099	68.72	680 ± 20
		Acetates, $ROCOCH_3$		
Allyl	6.064	5.202	42.06	11.5 ± 0.2
	6.019	5.782	56.00	34.8 ± 0.1
	7.080	6.278	68.72	93.6 ± 0.3
Benzyl	4.462	4.765	40.04	8.11 ± 0.03
	4.200	6.295	56.00	31.0 ± 0.2
	4.014	6.325	68.72	81 ± 1

ester trityl thiolacetate, which was shown to undergo alkyl–sulfur cleavage (path II), shows a much higher value for E, and a much more positive value for $\Delta S^{\ddagger}$, than the other esters examined. The *t*-butyl acetate, which was believed to hydrolyze by the same mechanism,[4] shows a similar contrast with the other members of its series. The relatively positive value of $\Delta S^{\ddagger}$ for these two compounds is in agreement with the idea that the rate-determining step is a dissociation, with an accompanying increase in the degrees of freedom of the transition state. The values for the other compounds do not show much variation with change in structure; a comparison of the relative rates of hydrolysis at 0° shows that the variations are over a fairly small range.

TABLE II

ARRHENIUS ENERGY, ENTROPY AND FREE ENERGY OF ACTIVATION FOR THE ACID-CATALYZED HYDROLYSIS OF $RSCOCH_3$ AND $ROCOCH_3$[a]

R	$RSCOCH_3$ E	$RSCOCH_3$ $\Delta S^{\ddagger}$	$RSCOCH_3$ $\Delta F^{\ddagger}$	$ROCOCH_3$ E	$ROCOCH_3$ $\Delta S^{\ddagger}$	$ROCOCH_3$ $\Delta F^{\ddagger}$
Allyl	16.3 ± 0.4	−32 ± 1	24	17.3 ± 0.4	−24 ± 1	23
Benzyl	19.8 ± 0.6	−21.6 ± 0.7	25	17.1 ± 0.1	−24.5 ± 0.2	23
Trityl	29.7 ± 0.6	16 ± 2	25	..	..	..
Methyl[b]	17.1	−29	25	15.7	−27	23
Ethyl	18.0	−27	25	16.0	−27	23
i-Butyl	20.5	−19	25	16.1	−27	23
i-Propyl	19.7	−22	25	16:3	−27	23
t-Butyl	20.7	−19	25	23.2	− 6	24

[a] Units: E and $\Delta E^{\ddagger}$, kcal./mole; $\Delta S^{\ddagger}$ cal./deg./mole. [b] $\Delta S^{\ddagger}$ and $\Delta F^{\ddagger}$ for this and the succeeding compounds were calculated from the data of Rylander and Tarbell.[4]

Alkaline Hydrolysis.—The basic hydrolysis of trityl thiolacetate did not lead to alkyl–sulfur cleavage with the formation of triphenylcarbinol; the product obtained from the hydrolysis solutions contained some triphenylcarbinol, but consisted mainly of a mixture of higher melting material, probably ditrityl disulfide and perhaps some triphenylmethyl peroxide.[9] Treatment of trityl mercaptan under the conditions of the hydrolysis also led to the formation of some triphenylcarbinol and a similar higher-melting mixture, showing that the triphenylcarbinol obtained in the hydrolysis probably arose by a secondary transformation of the trityl mercaptan.

TABLE III

SECOND-ORDER RATE CONSTANTS FOR THE ALKALINE HYDROLYSIS OF $RSCOCH_3$ AND $ROCOCH_3$ IN 62% AQUEOUS ACETONE

R	Initial concn. m./l. × 10^2 Ester	Initial concn. m./l. × 10^2 NaOH	Temp., °C	$k \times 10^3$ (m./l.$^{-1}$)/sec.
		Thiolacetates, $RSCOCH_3$		
Allyl	3.548	9.336	0.00	14.9 ± 0.6
	4.240	10.22	−11.22	3.62 ± 0.08
Benzyl	2.379	5.549	0.00	10.4 ± 0.4
	1.622	7.612	−11.18	3.1 ± 0.2
Trityl	0.293	3.313	0.00	2.2 ± 0.1
	.296	2.257	−11.2	0.56 ± 0.08
		Acetates, $ROCOCH_3$		
Allyl	4.983	8.131	0.00	9.0 ± 0.4
	6.111	10.21	−11.22	4.09 ± 0.05
Benzyl	3.017	5.777	0.00	9.8 ± 0.3
	5.446	7.571	−11.18	3.22 ± 0.05
Benzhydryl	2.830	6.405	0.00	1.78 ± 0.01

TABLE IV

ARRHENIUS ENERGY, ENTROPY AND FREE ENERGY OF ACTIVATION FOR THE BASE-CATALYZED HYDROLYSIS OF $RSCOCH_3$ AND $ROCOCH_3$[a]

R	$RSCOCH_3$ E	$RSCOCH_3$ $\Delta S^{\ddagger}$	$RSCOCH_3$ $\Delta F^{\ddagger}$	$ROCOCH_3$ E	$ROCOCH_3$ $\Delta S^{\ddagger}$	$ROCOCH_3$ $\Delta F^{\ddagger}$
Allyl	17.9 ± 0.5	− 3 ± 2	18	9.9 ± 0.5	−33 ± 2	18
Benzyl	16 ± 1	−12 ± 3	18	14.1 ± 0.4	−18 ± 2	18
Trityl	18 ± 2	− 5 ± 7	18	..	..	..
Methyl[b]	13.1	−22	19	12.2	−24	19
Ethyl	14.4	−19	19	12.2	−27	19
i-Butyl	18.5	− 6	20	12.4	−27	20
i-Propyl	17.6	− 9	20	12.2	−29	20
t-Butyl	17.0	−14	20	14.3	−29	22

[a] Units: $E^{\ddagger}$ and $\Delta F^{\ddagger}$, kcal./mole; $\Delta S^{\ddagger}$, cal./deg./mole. [b] $\Delta S^{\ddagger}$ and $\Delta F^{\ddagger}$ for this and the succeeding compounds were calculated from the data of Rylander and Tarbell.[4]

The quantitative data are given in Tables III and IV; the low value for allyl acetate may be noted, but it is apparently counteracted by a large negative value for $\Delta S^{\ddagger}$, and the rate of hydrolysis of allyl acetate is similar to the others in the series.

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[9] This product is reported to be formed in the decomposition of ditrityl disulfide (Blicke, THIS JOURNAL, 45, 1965 (1923)).

A tabulation of the relative rates of basic hydrolysis at 0° for the thiolacetates, taking the ethyl compound as 1.00, shows the following order: allyl > benzyl > methyl > ethyl > trityl > *i*-propyl > *i*-butyl > *t*-butyl. The total spread is only from 3.56 for allyl to 0.10 for *t*-butyl, and the order of decreasing rate is the order of increasing electron-supply through the sulfur atom.[10]

A somewhat similar series is followed in the oxygen series: methyl > benzyl > allyl > ethyl > *i*-butyl > benzhydryl > *i*-propyl > *t*-butyl. In this case the spread is greater than in the sulfur series, and the relative rates range is from 2.29 (methyl) to 0.0052 (*t*-butyl).

Acknowledgment.—We are indebted to Dr. Peter Hawkins for interesting discussions.

Experimental

Thioacetic Acid.—Thioacetic acid (b.p. 85–90°) was prepared in an average yield of 31% by the action of acetyl chloride on a saturated solution of hydrogen sulfide in dry pyridine.[11]

Allyl Thiolacetate.—To a solution of sodium methoxide in methanol prepared from 3.02 g. of sodium and 36 cc. of methanol, 10.0 g. of thioacetic acid was added dropwise with cooling. Allyl chloride (9.0 g.) was then added dropwise, and the mixture was stirred for 45 minutes. After standing overnight, the mixture was poured into ice-water, extracted three times with ether, and the extracts were washed with iced sodium bicarbonate solution. After the solution was dried and the solvent removed, allyl thiolacetate boiling at 29–29.5° (9 mm.) was obtained in 66% yield. Redistillation yielded material of the following properties[12]: b.p. 53–54° (29 mm.); $n^{25}D$ 1.4797; d^{25}_{25} 0.9878.

Anal. Calcd. for C_5H_8OS: C, 51.69; H, 6.94; *M*D, 32.80; neut. equiv., 116.2. Found: C, 51.73; H, 6.64; *M*D, 33.39; neut. equiv., 114.6.

Benzyl Thiolacetate.—Benzyl mercaptan (50 g.) was refluxed with 200 cc. of acetic anhydride for 12 hours. The ester was isolated as above,[13] b.p. 75.5–76.8° (0.7–0.8 mm.); $n^{25}D$ 1.5565.

Anal. Calcd. for $C_9H_{10}OS$: C, 65.02; H, 6.05. Found: C, 64.52; H, 5.96.

Trityl Thiolacetate.—To a methanol-free sample of sodium methoxide, prepared from 1.27 g. of sodium, thioacetic acid (4.2 g.) in 8 cc. of dry benzene was added, followed by 14.0 g. of trityl cloride (m.p. 106–109°) dissolved in 25 cc. of dry benzene. The mixture was stirred 90 minutes. After standing overnight, it was worked up as above. The product (8 g.) was obtained by crystallization from pentane, m.p. 137–139°, and 1 g. of additional material with lower m.p., was isolated from the filtrate. The combined sample melted, after four recrystallizations from benzene–pentane, at 146.9–147.5° (uncor.).[14]

Anal. Calcd. for $C_{21}H_{18}OS$: C, 79.21; H, 5.70; S, 10.07. Found: C, 79.38; H, 5.91; S, 10.31.

Other esters used were synthesized or purchased, and purified by distillation through a good column, or by recrystallization, until the physical properties were not changed by further treatment. Purity was checked in most cases by carbon–hydrogen analysis or neutral equivalent determinations.

Acetone (C.P.) was dried over anhydrous potassium carbonate and distilled through a 2-ft. helix-packed column. It gave a negative Tollens test.

PROPERTIES OF ACETATES, CH_3COOR

R	B.p. or m.p., °C. Obsd.	B.p. or m.p., °C. Lit.	n^tD Obsd.	t, °C. Obsd.	n^tD Lit.	t, °C. Lit.
Allyl	102.3–103.2	103.5[a]	1.4046	18	1.4048	18[a]
Benzyl	60.7–61.2 (4.5 mm.)	93 (10 mm.)[a,b]	1.5013	21	1.5032	19.9[a,b]
Benzhydryl[d]	40.5–41.5	40[c]				
Trityl[f]	81.5–83	87–88[e]				

[a] Olsson, *Z. physik. Chem.*, **125**, 246 (1927). [b] Tromp, *Rec. trav. chim.*, **41**, 298 (1922). [c] Dimroth and Schweizer, *Ber.*, **56**, 1384 (1923). [d] *Anal.* Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.79; H, 6.38. [e] Gomberg, *Ber.*, **35**, 1835 (1902). [f] Neut. equiv., calcd. for $C_{21}H_{18}O_2$: 302.4. Found: 299 ± 3. (A correction for blank determination was applied.)

Rate Runs.—Runs at 30–70° were made in thermostats accurate to 0.05° or better. The thermostat used at −11° consisted of a 5-l. dewar, containing a mercury thermo regulator, stirrer, and a 40-watt bulb as a heater. The bath liquid, a brine solution, was cooled by pumping it through a copper coil in a second dewar containing Dry Ice and ethylene glycol. The temperature, which could be controlled within 0.05°, was measured by a low temperature mercury thermometer, which was calibrated at 0° in ice-water, then compared with two Beckmann thermometers set in sequence from 0 to −12°.

The hydrochloric acid or sodium hydroxide solutions in 62% aqueous acetone were made by weight, from 0.5 molal solutions, boiled water and acetone. The solutions were kept in an ice-bath until used. The basic solutions were used within one or two hours; the acidic solutions could be kept overnight. The titer of the solutions agreed within 2% of the calculated value.

Procedure A.—The acid-catalyzed hydrolyses were run in sealed tubes at 40 to 69°. A sample of the ester was weighed into a 125-ml. glass-stoppered flask; the 62% aqueous acetone solution of hydrochloric acid was added, and the solution was weighed. The test-tubes which had previously been cleaned in an acid-bath, rinsed with dilute ammonia and distilled water, dried and constricted, were filled with a pipet. The tubes were chilled in ice-water, sealed off and thermostated.

Procedure B.—For the alkaline hydrolyses with the exception of *t*-butyl acetate, the esters were weighed in sealed glass bulbs which were broken under a known weight of solvent after both ester and solvent had been properly thermostated. The runs on *t*-butyl acetate were made in sealed tubes as in procedure A.

Procedure C.—Due to the slow rate of solution of the trityl thiolacetate, methods A and B were not applicable. The requisite amounts of 0.5 molal acid or base solution and boiled distilled water were weighed out and the thiolacetate solution in acetone made up by weight. In the alkaline hydrolysis the two solutions were thermostated and the aqueous solution then added to the acetone solution. The weight of the aqueous solution was determined by difference. In the acid-catalyzed hydrolysis, the two solutions were mixed at room temperature, then sealed in ampoules.

The ampoules were quenched for five minutes in ice-water before opening, then a 5-cc. aliquot was withdrawn. The acidic solution was titrated directly with base. An aliquot of the basic solutions was delivered into excess acid, then back-titrated. Phenolphthalein was used as an indicator for the acetates, and thymol blue for the thiolacetates. A 5-ml. Koch buret was used for the titrations. During each run one aliquot was weighed. The titer of the solutions could not be determined at the completion of the run except for the acid-catalyzed hydrolysis of the acetates where it agreed with the calculated value within 2%.

Treatment of Data.—The specific rate constants in Tables I and III and the *E* for the acid-catalyzed hydrolysis were calculated by the methods of the least squares. The *E* for the basic hydrolyses were calculated directly from the data for the two temperatures. The $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were obtained from the equation[8]

$$k = \frac{\mathbf{k}T}{\mathbf{h}} e^{\frac{-\Delta H^\ddagger}{RT}} e^{\frac{\Delta S^\ddagger}{R}}$$

Acid-catalyzed Hydrolysis of Benzyl Thiolacetate.—Benzyl thiolacetate (1.5 g.) in 62% aqueous acetone was heated

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[10] Allyl and benzyl groups can act as electron sinks, as shown by their effect on the dissociation constants of acetic acid (Dippy, *Chem. Revs.*, **25**, 180 (1939)).

[11] Sunner and Nilson, *Svensk. Kem. Tid.*, **54**, 163 (1942).

[12] Allen, U. S. Patent 2,212,895, reports the following physical constants for allyl thiolacetate: b.p. 136–136.8°; $n^{20}D$ 1.435; d^{20}_4 1.0325.

[13] The b.p. is reported by Smythe (*J. Chem. Soc.*, **122**, 1405 (1922)) as 248° at atmospheric pressure.

[14] The reported m.p. varies from 138–141° (*e.g.*, Vorländer and Mittag, *Ber.*, **46**, 3457 (1913)).

in a sealed tube at 68.8° for a period of ten half-lives, the solution being 0.176 *M* in ester and 0.122 *M* in hydrochloric acid. The acetone was removed by distillation, and the product was extracted with ether. The solution was dried and the solvent distilled. Distillation of the residue yielded 0.63 cc. of material, b.p. 90–110° (28–32 mm.). The 3,5-dinitrobenzoate of the material melted after two recrystallizations from ethanol,[15] at 117–118°; since benzyl 3,5-dinitrobenzoate is reported[16] to melt at 113°, the product was analyzed to be certain that it was the thiolester.

Anal. Calcd. for $C_{14}H_{10}N_2O_5S$: C, 52.82; H, 3.17. Found: C, 53.04; H, 3.23.

Acid-catalyzed Hydrolysis of Trityl Thiolacetate.—The product which crystallized from the aliquot titrated at the completion of a run was filtered and washed with water. It melted at 156–159°. When mixed with triphenylcarbinol it melted at 158–160°.

Alkaline Hydrolysis of Trityl Thiolacetate.—A 62% aqueous acetone solution, 0.041 *M* in sodium hydroxide and 0.0056 *M* in trityl thiolacetate was prepared from 0.178 g. of the thiolacetate. The solution was kept in an ice-water mixture for ten hours, then acidified with hydrochloric acid. The acetone was removed under reduced pressure. The oil which separated was extracted with C.P. ether, and the solution dried, then the solvent removed. The residual oil yielded only a minute crystalline product upon standing in the refrigerator; it melted at 183°. A semi-solid product was obtained from the remainder of the oil by crystallization from ethanol and water. By fractional crystallization from C.P. benzene and pentane, and decolorization with Filtrol, three fractions were obtained, only one of which was pure. The low melting fraction, 77–78°, upon recrystallization melted at 95–108°, then formed a higher melting product. A product melting at 177–178°, after two recrystallizations from benzene and pentane, was lost when a micro-crystallization tube broke in the centrifuge. The third product from the filtrate of the 177–178° material after recrystallization melted at 155–159°, and mixed with triphenylcarbinol melted at 155–159.5°.

Trityl Mercaptan in Alkaline 62% Aqueous Acetone.—A 62% aqueous acetone solution, 0.041 *M* in sodium hydroxide and 0.0023 *M* in mercaptan, was prepared from 0.063 g. of trityl mercaptan.[17] The solution was kept at 0° for ten hours and treated in the same manner as the thiolacetate. The melting point of the few crystals which formed by refrigerating the oil was 175–185°. An oily solid was finally obtained from the oil by recrystallization from ethanol and water. Fractional crystallization from benzene and pentane and treatment with Filtrol of the benzene solution gave triphenylcarbinol, melting after two recrystallizations at 162°. The melting point when mixed with commercial triphenylcarbinol was 160°. Subsequent fractions gave only impure carbinol with melting points of 156–160° and 155–159°.

Trityl Mercaptan in Dilute Hydrochloric Acid Solution.—Slightly impure trityl mercaptan (0.25 g.), m.p. 100–107°, dissolved in 104 g. of 62% aqueous acetone, 0.012 *M* in hydrochloric acid was refluxed 25 hours (about 10 half-lives) on a steam-bath. After the acetone was removed by distillation, the yellow oil which separated was extracted with ether. The crystalline product was recovered in 68% yield and melted at 75–80°. Crystallization from chloroform and hexane gave a 50% yield (based on the original wt. of mercaptan taken) of trityl mercaptan, m.p. 103–109°.

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[15] Wertheim, THIS JOURNAL, **51**, 366 (1929), reports benzyl 3,5-nitrobenzoate to melt at 119–120.

[16] Huntress and Mulliken, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 471.

[17] The mercaptan, m.p. 106–107°, was generously given to us by Dr. N. Kharasch of the University of Southern California.

ROCHESTER 3, NEW YORK RECEIVED JUNE 19, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FRESNO STATE COLLEGE]

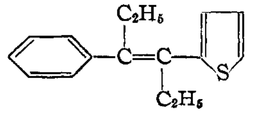
Some Thiophene Analogs of Diethylstilbestrol

BY W. R. BIGGERSTAFF AND OWEN L. STAFFORD

Two thiophene analogs of diethylstilbestrol, IIIa and IIIb, have been prepared. Physiological tests indicate that IIIa produces 50% estrus (rats) in 100γ doses (100% at 250γ). The benzene analog, 4-hydroxy-α,α'-diethylstilbene, has been reported[5b] to produce only trace activity at 100γ.

Other workers[1] have observed that the substitution of a 2-thienyl radical for a phenyl radical in certain physiologically active compounds may result in an enhanced activity.

During the course of a previous attempt to correlate structure and estrogenic activity[2] the effect of a 2-thienyl group in place of a phenyl group in α,α'-diethylstilbene was examined. The thiophene analog I[3] was tested and found to possess a low order of estrogenic activity.[4]



I

The conclusion was reached by these workers[2] that the substitution had resulted in a lowering of the estrogenic activity. However, in view of the relatively low estrogenic action of either α,α'-diethylstilbene[5a] or I this evidence appeared inconclusive and it seemed to us that additional data on related compounds might be useful.

Since the introduction of a 4-hydroxyl group into the α,α'-diethylstilbene nucleus greatly enhances its activity,[5b] it was thought that a similar introduction of the hydroxyl group into compound I should also produce an increased activity. Compounds IIIa and IIIb have now been prepared by following a previously described scheme.[6]

The acid chloride of α-(*p*-acetoxyphenyl)-butyric acid was condensed with thiophene to give, after hydrolysis of the acetate, the hydroxy ketone IIa

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[1] (a) H. Y. Lew and C. R. Noller, THIS JOURNAL, **72**, 5715 (1950); (b) A. W. Weston, *ibid.*, **69**, 980 (1947); (c) F. F. Blicke and M. U. Tsao, *ibid.*, **66**, 1645 (1944); (d) Buu-Hoï, Nguyen-Hoán and D. Lavit, *J. Chem. Soc.*, 2130 (1950).

[2] L. Corre, Buu-Hoï, D. Guettier, A. Lacassagne, J. Lecoq, R. Royer and G. Rudali, *Bull. soc. chim. biol.*, **28**, 716 (1946).

[3] For the preparation of this compound (as an oil) see Buu-Hoï and Hiong-Ki-Wei, *Compt. rend.*, **220**, 175 (1945). Other thiophene analogs of stilbene have been reported (see ref. 1d).

[4] A 10-mg. dose produced estrus in mice.

[5] (a) M. Rubin and H. Wishinsky, THIS JOURNAL, **66**, 1948 (1944), have reported α,α'-diethylstilbene to be inactive at 1000 γ in rats; (b) 4-hydroxy-α,α'-diethylstilbene produces 100% estrus in rats at 1000 γ and only a trace at 100 γ according to E. C. Dodds, L. Golberg, W. Lawson and R. Robinson, *Proc. Roy. Soc.* (*London*), **B127**, 140 (1939).

[6] A. L. Wilds and W. R. Biggerstaff, THIS JOURNAL, **67**, 789 (1945).