acid. The benzyl ether crystallized out on cooling as long, yellow needles without melting point. Yield, 65%.

Subst. (I) 0.1653, (II) 0.1832; cc. 0.1 *N* $AgNO_3$. (I) 8.74, (II) 9.67.
Calc. for $C_{15}H_7O_3NI_4$: I, 67.08%. Found: (I) 67.11, (II) 66.99.

Acetate.—5 g. of pure tetraiodophthaloxime were dissolved in 75 cc. acetic anhydride by heating below the boiling point for about 40 minutes. The acetate crystallized out on cooling in bright yellow needles. It was purified from ethyl acetate.

Subst. (I) 0.2043, (II) 0.1699; cc. 0.1 *N* $AgNO_3$. (I) 11.52, (II) 9.59.
Calc. for $C_{10}H_3O_4NI_4$: I, 71.62%. Found: (I) 71.60, (II) 71.62.

Benzoate.—8 g. of pure tetraiodophthaloxime were dissolved in 65 cc. of benzoyl chloride 135–150°, and heated at this temperature for 30 minutes. The benzoate was precipitated by adding alcohol, filtered, and washed free from ethyl benzoate. The yellow needles showed no melting point.

Subst. (I) 0.5980, (II) 0.6311; cc. 0.1 *N* $AgNO_3$. (I) 31.06, (II) 32.61.
Calc. for $C_{15}H_5O_4NI_4$: I, 65.86%. Found: (I) 65.92, (II) 65.59.

PITTSBURGH, PA.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF SMITH COLLEGE.]

ON THE ADDITION OF SODIUM ACETOACETIC ESTER TO THE AROMATIC MUSTARD OILS.

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Introduction.

In the course of an investigation of the action of phenylhydrazine and hydroxylamine on thio derivatives it became necessary to prepare the monothioanilide of acetomalonic ester, $CH_3COCH(CSNHC_6H_5)COOC_2H_5$. No experimental details were found for the preparation of this ester and since few compounds of this type have been made, a short study was made of their synthesis and reactions.

Michael[1] first pointed out that thioanilides may be built up, through the sodium derivative, by the action of sodium malonic ester on the mustard oils. With phenyl mustard oil the reactions were expressed as follows:

$$CHNa(COOC_2H_5)_2 + C_6H_5NCS = CH(CSNa.NC_6H_5)(COOC_2H_5)_2$$

$$CH(CSNa.NC_6H_5)(COOC_2H_5)_2 + \text{acid} \longrightarrow CH(CSNHC_6H_5)(COOC_2H_5)_2$$

A similar reaction would be expected with any ester containing an acidic methylene group. Thus Ruheman[2] found that sodium cyanomalonic ester as well as sodium malonic ester added to phenyl mustard oil forming thioanilides. Sodium acetoacetic ester[3] also reacts with phenyl mustard oil.

[1] *J. prakt. Chem.*, [2] **35**, 450 (1887).

[2] *J. Chem. Soc.*, **93**, 621 (1908).

[3] Michael, *J. prakt. Chem.*, [2] **60**, 286 (1899).

Discussion of Results.

It has been found that sodium acetoacetic ester reacts readily with phenyl, the three tolyl, *p*-bromo and β-naphthyl mustard oils. The ethyl and benzyl derivative of sodium acetoacetic ester reacts less readily with phenyl mustard oil. The additions, with the exception of the substituted esters go readily at room temperature, although to increase the speed of reaction the mixtures were usually heated in a water bath. Since the mustard oils react with alcohol to form substituted thio urethanes ether was used as a diluent. For this reason sodium ethoxide was not used to prepare sodium acetoacetic ester, although considerable trouble was experienced in the preparation by the use of metallic sodium because of unchanged metal.

The reaction between mustard oil and the sodium compound takes place as follows:

$$CH_3COCHNaCOOC_2H_5 + RNCS = CH_3COCH(CSNa.NR)COOC_2H_5$$

The attachment of sodium to sulfur was established by condensing the sodium derivative with ethyl iodide and heating the resulting oil with acid. It decomposed in such a way as to form ethyl mercaptan, which was recognized by its repulsive odor. An isomer of this substance was prepared by using the ethyl derivative of sodium acetoacetic ester with phenyl mustard oil, a reaction which confirms the above interpretation of the addition. The sodium addition product of the ester and mustard oil on neutralization with acid isomerizes, the hydrogen shifting from sulfur to nitrogen, to form a thioanilide.

$$CH_3COCH(CSNa.NC_6H_5)COOC_2H_5 + HCl \longrightarrow CH_3COCH\text{-}(CSHNC_6H_5)COOC_2H_5 \longrightarrow CH_3COCH(CSNHC_6H_5)COOC_2H_5.$$

This view is supported by the fact that these thioanilides condense readily with hydroxylamine and phenylhydrazine[1] splitting out hydrogen sulfide.

The thioanilides resulting from the action of phenyl mustard and *p*-substituted phenyl mustard oil together with the naphthyl derivative undergo acid decomposition easily and smoothly with alkali.

$$CH_3COCH(CSNHR)COOC_2H_5 + H_2O = CH_2(CSNHR)COOH + CH_3COOH + C_2H_5OH.$$

The reaction goes so readily that dilute alkali almost instantly brings about the hydrolysis. The resulting acid when heated decomposes at its melting point with evolution of carbon dioxide, changing almost quantitatively into a thioacetoanilide.

$$CH_2(CSNHR)COOH \longrightarrow CH_3CSNHR + CO_2.$$

While the introduction of substituents, both positive and negative, in phenyl mustard oil has no apparent effect on the addition of sodium

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[1] These results will be published later.

acetoacetic ester, the behavior of the resulting products is modified. Thus the introduction of a methyl group in the ortho and para position results in compounds which are unstable and even with careful treatment, ketonic hydrolysis takes place.

$$CH_3COCH(CSNHC_6H_4CH_3)COOC_2H_5 + H_2O = CH_3COCH_2CSNHC_6H_4CH_3 + CO_2 + C_2H_5OH.$$

Hence while phenyl mustard oil and its *p*-derivatives form esters which can be isolated unchanged, although they undergo acid hydrolysis on treatment with alkali, *o*- and *m*-tolyl mustard oils form compounds which decompose so readily that only the hydrolysis products can be isolated. The resulting ketones readily undergo further hydrolysis either with acid or alkali.

$$CH_3COCH_2CSNHC_6H_4CH_3 + H_2O = CH_3COOH + CH_3CSNHC_6H_4CH_3.$$

The replacement of hydrogen in the methylene group of acetoacetic ester by an alkyl substituent lessens the ease of addition to phenyl mustard oil, but the resulting compound is much more stable toward alkali and is decomposed only by prolonged treatment at high temperature. The benzyl derivative of sodium acetoacetic ester is still less reactive toward mustard oil. The compound formed however, is apparently a polymerized decomposition product of the expected ester.

Experimental.

Preparation of Materials.—The mustard oils were prepared by the well-known method[1] of condensing the corresponding amine with carbon bisulfide to form symmetrical disubstituted thioureas, which were decomposed by short heating with acid. The product in each case was distilled in steam and further purified by redistillation. Notwithstanding these precautions a small amount of crystalline material always separated out, on standing, from the liquid mustard oils. This was especially true with *o*-tolyl mustard oil which deposited crystals after three distillations, a characteristic that has been noted by other investigators.[2] The deposit from a lot of phenyl mustard oil was filtered out, washed and dried in vacuum. It melted at 152–153°, and when heated with concentrated hydrochloric acid formed phenyl mustard oil, proving the substance to be unchanged thiocarbanilide, which must have been carried over mechanically in the distillations.

The acetoacetic ester was converted into the sodium derivative by the use of granulated sodium.[3] The product always contained some unchanged metal and ester because the sodium derivative, which is not very soluble

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[1] *Beilstein,* [3] **2,** 388; Girard, *Ber.,* **6,** 445 (1873); Weith, Landolt, *Ibid.,* **8,** 719 (1876); Hofmann, *Ibid.,* **15,** 986 (1882).

[2] Mainzer, *Ber.,* **16,** 2017 (1883).

[3] Bruhl, *Ibid.,* **35,** 3516 (1902).

in ether, had a tendency to enclose the metallic sodium and prevent further reaction. This difficulty was not experienced with the ethyl derivative of the ester which forms a sodium compound readily soluble in ether.

Ethylacetomalonate Monothioanilide, $CH_3COCH(CSNHC_6H_5)COOC_2H_5$.—Ten grams of acetoacetic ester were converted into the sodium derivative in 8–10 volumes of dry ether, to which were added 10.4 g. of phenyl mustard oil. The sodium compound which had largely separated out, went into solution in a few minutes and at the same time a viscid pale yellow oil began to form on the sides of the flask. This deposit later became crystalline and subsequently the new substance separated directly as a solid. Ice water was poured into the mixture after twelve hours' standing at room temperature. The aqueous layer was extracted again with ether and then added drop wise, with stirring, to cold well diluted hydrochloric acid. The heavy yellow oil which formed hardened slowly to a crystalline mass. This was washed, recrystallized from alcohol and dried in a vacuum desiccator. Yield of crude product, about 12 g.

0.2 subst. gave 9.8 cc. N_2 at 17° and 756 mm.
Calc. for $C_{13}H_{15}O_3NS$: N, 5.3. Found: N, 5.7.

Properties of Ethylacetomalonate Monothioanilide.—It is readily soluble in alcohol, benzene, acetone, ammonium hydroxide and sodium hydroxide solution. It crystallizes from alcohol in pale yellow, prismatic needles, which melt slowly at 82–83°. The thioanilide is very unstable toward alkaline reagents, more stable with the mineral acids but easily decomposed by the latter if heated. It is extremely soluble in ammonium hydroxide, from which an oil separates on standing.

Action of Hydrochloric Acid.—A small amount of the substance was heated with concentrated hydrochloric acid for a few minutes. Hydrogen sulfide was evolved and then the pleasant odor of ethyl acetate was observed. The acid solution was then evaporated to dryness and the crystalline residue identified as aniline hydrochloride. An alcoholic solution of silver nitrate on warming decomposed the thio derivative with the formation of silver sulfide. The alcohol was oxidized to acetaldehyde.

Action of Sodium Hydroxide.—Two grams of the substance were dissolved in a small volume of warm sodium hydroxide solution. The mixture was cooled and cautiously neutralized with hydrochloric acid. The bulky precipitate of brilliant yellow plates which formed was filtered and dried. The new substance melted with evolution of carbon dioxide at 91–92° and formed a white precipitate with silver nitrate which immediately blackened. The oil from the carbon dioxide evolution hardened to a solid, which was crystallized from alcohol in yellow prisms melting at 75°. These characteristics identified the first derivative as the thioanilide of malonic acid, a substance which Ruheman[1] obtained from another ester.

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[1] *J. Chem. Soc.*, **93**, 624 (1908).

It is formed in this case by the acid hydrolysis of the acetomalonic ester derivative as follows:

$$CH_3COCH(CSNHC_6H_5)COOC_2H_5 + 2H_2O = CH_3COOH + C_2H_5OH + CH_2(CSNHC_6H_5)COOH$$

Thioacetoacetyl-*o*-toluide, $CH_3COCH_2CSNHC_6H_4CH_3$.—Five grams of *o*-tolyl mustard oil were added to sodium acetoacetic ester. The mixture was refluxed for several hours and the viscid oil which separated out was dissolved in cold water and acidified with the usual precautions. The heavy yellow oil which formed, crystallized in a few minutes. It was recrystallized from alcohol and dried in a vacuum desiccator. Yield of crude product, about 7 g.

0.1 g. gave 6.2 cc. N_2 at 21° and 754 mm.
Calc. for $C_{11}H_{13}ONS$: N, 6.8. Found: N, 7.0.

Attempts to obtain the acetomalonate derivative failed; instead ketone hydrolysis of the expected compound always took place.

Properties of Thioacetoacet-*o*-toluide.—It dissolves readily in the usual solvents, crystallizing from alcohol in slender, nearly colorless needles which melt slowly at 73–75°. It decomposes somewhat on long standing and the sharp characteristic odor of acetic acid is developed. It is very easily decomposed by alkali.

Action of Hydrochloric Acid.—Two grams of the toluide were heated with a few cc. of concentrated hydrochloric acid for a few minutes. It was then cooled and the crystalline mass separated from the acid. Alcohol was added to the latter and on warming the pleasant odor of ethylacetate was given off, proving acetic acid to be one of the products of the reaction. The precipitate was recrystallized several times from ligroin, finally separating as shining (nearly) colorless needles which melted at 91–92°.

0.1 g. gave 7.8 cc. N_2 at 21° and 756 mm.
Calc. for $C_9H_{11}NS$: N, 8.5. Found: N, 8.8.

The substance was readily soluble in cold alkali, from which it could be precipitated unchanged by acid. It appeared to be thioacetyl-*o*-toluide.

$$CH_3COCH_2CSNHC_6H_4CH_3 + H_2O = CH_3COOH + CH_3CSNHC_6H_4CH_3.$$

This thiotoluide was first prepared by Wallach[1] who described it as melting at 67–68°. It was also obtained by dissolving acetoacetic thiotoluide in cold alkali and neutralizing carefully with acid. The ether layer from the original preparation, on evaporation deposited several large crystals of the thioacetyl toluide, indicating the extreme sensitiveness of acetoacetyl thiotoluide toward alkali.

Thioacetoacetyl-*m*-toluide, $CH_3COCH_2CSNHC_6H_4CH_3$.—One gram of acetoacetic ester was converted into the sodium derivative and the molecular equivalent of *m*-tolyl mustard oil added. The mixture was refluxed

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[1] *Ber.*, **13**, 529 (1880).

for an hour, the voluminous crystalline precipitate shaken with ice water and treated with acid in the usual manner. The yellow oil which separated out hardened to a crystalline mass, which was digested with a little ether and dried on a porous plate. It melted at 83–84°.

0.1 g. subst. gave 6.5 cc. N_2 at 22° and 754 mm.
Calc. for $C_{11}H_{13}ONS$: N, 6.8. Found: N, 7.3.

Action of Sodium Hydroxide.—The new compound was dissolved in warm sodium hydroxide solution, cooled and neutralized with acid. An oil separated out which did not harden on standing.

Ethylacetomalonate Monothio-*p*-toluide, $CH_3COCH(CSNHC_6H_4CH_3)COOC_2H_5$.—Five grams of *p*-tolyl mustard oil were added to the equivalent amount of sodium acetoacetic ester and the mixture kept at room temperature overnight. A bulky, crystalline precipitate settled out. This was filtered, washed with dry ether and dried in vacuum. Most of this substance was dissolved in ice water, and added slowly to dilute acid. A yellow oil separated out which subsequently solidified. It was recrystallized and dried in a vacuum. Yield, 4–5 g.

0.2 g. subst. gave 9 cc. N_2 at 20° and 762 mm.
Calc. for $C_{14}H_{17}O_3NS$: N, 5.0. Found: N, 5.1.

Properties of Ethylacetomalonate Monothio-*p*-toluide.—It is readily soluble in alcohol, benzene, sodium hydroxide solution and ammonium hydroxide. It crystallizes from alcohol in shining, diamond-shaped tablets, which melt at 81°. The crystals are nearly colorless, although the alcohol solution is decidedly yellow.

Sodium Salt of Ethylacetomalonate Monothio-*p*-toluide, $CH_3COCH(CSNa.NC_6H_4CH_3)COOC_2H_5$.—This derivative as prepared above, separated in small, colorless needles which melted at 61–62° with decomposition.

0.1 g. subst. formed 0.0225 g. Na_2SO_4.
Calc. for $C_{14}H_{16}O_3NSNa$: Na, 7.64. Found: Na, 7.54.

Action of Sodium Hydroxide.—Two grams of the toluide ester were dissolved in a small volume of warm sodium hydroxide solution and carefully neutralized, after cooling, with acid. The brilliant yellow crystals which immediately filled the beaker, were filtered, recrystallized from water and dried in vacuum.

0.1 g. subst. gave 6.1 cc. N_2 at 23° and 756 mm.
Calc. for $C_{10}H_{11}O_2NS$: N, 6.7. Found: N, 6.8.

The new compound was malonic acid monothio-*p*-toluide,

$$CH_2(CSNHC_6H_4CH_3)COOH.$$

Properties of Malonic Acid Monothio-*p*-toluide.—It crystallizes from hot water in long, colorless, flat needles which melt with foaming, due to the evolution of carbon dioxide, at 97°. It has a very bitter taste, a characteristic shared by the parent substance from which it is derived and the thiotoluide into which it is easily changed by heat. Silver nitrate and mercuric chlorides form amorphous white precipitates which darken on standing.

Action of Heat on Malonic Acid Monothio-*p*-toluide.—A small amount of the substance was heated slightly above the melting point in a glycerine bath, until the evolution of carbon dioxide was completed. The resulting oil immediately solidified on cooling and was recrystallized from alcohol in long, shining needles which melted at 129.5–130.5°.

0.1 g. subst. gave 8.0 cc. N_2 at 23° and 756 mm.
Calc. for $C_9H_{11}NS$: N, 8.5. Found: N, 8.8.

The product was thioaceto-*p*-toluide, identical with the preparation of Wallach.[1]

Ethylacetomalonate Monothio-*p*-bromoanilide, $CH_3COCHCSNHC_6H_4$-$BrCOOC_2H_5$.—Three grams of *p*-bromophenyl mustard oil were added to the equivalent amount of sodium acetoacetic ester, suspended in ether, and kept at room temperature for twelve hours, during which time a yellowish white crystalline product formed. The mixture was shaken with water and treated with acid in the usual way. The yellow oil separating out hardened, on standing overnight in an ice chest. Yield, 4 g. The product was digested with a little ether and dried in a vacuum. It melted at 81–83°.

0.2 g. subst. gave 7.8 cc. N_2 at 23° and 758 mm.
Calc. for $C_{13}H_{14}O_3NSBr$: N, 4.1. Found: N, 4.4.

Action of Sodium Hydroxide.—Two grams of the ester were dissolved in a little warm sodium hydroxide solution, cooled and neutralized with hydrochloric acid. The precipitate was filtered, recrystallized from water and dried in vacuum.

0.2 g. subst. gave 9.4 cc. N_2 at 18° and 760 mm.
Calc. for $C_9H_8O_2NSBr$: N, 5.1. Found: N, 5.4.

Evidently malonic acid monothio-*p*-bromoanilide, $CH_2(CSNHC_6H_4Br)$-COOH was formed as a result of the hydrolysis.

Properties of Malonic Acid Monothio-*p*-bromoanilide.—It is easily soluble in alcohol, benzene, sodium and ammonium hydroxide solutions. The bromoanilide crystallizes from water in cream-colored flattened needles and plates. It is impossible to ascertain accurately the melting point, since a new substance of high melting point is formed when this derivative is heated. If heated slowly it changes imperceptibly to the new substance, but if plunged into a bath heated to 131°, it partially melts with foaming, then rehardens. The bromo derivative forms an unstable white silver salt which changes, on standing, to silver sulfide.

Thioaceto-*p*-bromoanilide, $CH_3CSNHC_6H_4Br$.—One gram of the malonic acid thiobromoanilide was heated in an oil bath to 150° for a few

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[1] *Ber.*, 13, 529 (1880).

minutes. The product was recrystallized from alcohol in colorless, six-sided, narrow plates which melted at 153°.

0.1 g. subst. gave 5.5 cc. N_2 at 20° and 764 mm.
Calc. for C_8H_8NSBr: N, 6.1. Found: N, 6.3.

Ethylacetomalonate Monothio-β-naphthylamide, $CH_3COCH(CSNHC_{10}H_7)COOC_2H_5$.—1.5 g. of β-naphthyl mustard oil were added to the corresponding amount of sodium acetoacetic ester in ether. The yellowish white precipitate which formed after twelve hours' standing was treated in the customary manner, resulting in a heavy yellow oil which did not solidify on standing. No analysis was made of the substance because of the uncertainty of the purification and the small amount available, but the behavior with alkali afforded a check on the compound so that there is little doubt that the above interpretation is correct.

Action of Sodium Hydroxide.—The oil was dissolved in warm sodium hydroxide solution and carefully neutralized with acid. The resulting voluminous precipitate was recrystallized from water in pale yellow plates and flattened needles which melted at 87–89° with foaming.

0.1 g. subst. gave 5.2 cc. N_2 at 21° and 758 mm.
Calc. for $C_{13}H_{11}O_2NS$: N, 5.7. Found: N, 5.9.

The new derivative is malonic acid monothio-β-naphthylamide, $CH_2(CSNHC_{10}H_7)COOH$. The fragment of material remaining was heated on a water bath until the evolution of carbon dioxide had ceased. The yellow oil hardened on cooling to a crystalline mass which melted at 119–122° and was an impure form of thioaceto-β-naphthylamide. This substance when pure melts at 145–146°.[1]

Ethylacetoethylmalonate Monothioanilide, $CH_3COC(C_2H_5)(CSNHC_6H_5)COOC_2H_5$.—Ten grams of the ethyl derivative of ethylacetoacetic ester were converted into the sodium derivative and 8.6 g. of phenyl mustard oil added to the clear ether solution of the ester. A compact crystalline precipitate separated out on the sides of the flask after it had been refluxed two hours. It was heated for another hour and the solid filtered, washed with dry ether and dried over calcium chloride. Most of the sodium derivative was treated with acid, observing the usual precautions and the ester separated in good yield as an oil which did not harden on standing. The sodium derivative was used for analysis.

0.3415 g. subst. gave 0.0741 Na_2SO_4.
Calc. for $C_{15}H_{18}O_3NSNa$: Na, 7.3. Found: Na, 7.1.

Properties of Ethylacetoethylmalonate Monothioanilide.—The substance is an oil which is miscible with organic solvents, also sodium or potassium hydroxide. It is much more stable toward alkali than the corresponding acetomalonate derivative and is not hydrolyzed by cold caustic

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[1] Sullwald, *Ber.*, 21, 2627 (1888).

alkali solutions. Boiling hydrochloric acid acted slowly on the ester, but without the formation of crystalline compounds.

Action of Potassium Hydroxide.—Two grams of the ester were dissolved in a rather concentrated water solution of potassium hydroxide and refluxed for several hours, during which time an oil gradually separated out. The mixture was distilled with steam and a small amount of a colorless oil with a penetrating but not unpleasant odor came over and dissolved in the distillate. The original mixture still retained a red oil which solidified on cooling. It was filtered, washed and crystallized several times from ligroin, finally separating in colorless, shining, square plates which melted at 94–95°. The filtrate from the first separation when acidified, evolved hydrogen sulfide and a copious yellow precipitate formed. This was separated and recrystallized from water in glistening, irregular plates. The new substance when heated melted at 150–151° with foaming, due to evolution of carbon dioxide and changed to a compound which melted at 94–95°, thus proving the identity of the latter with the substance insoluble in alkali. The presence of both sulfur and nitrogen was proved in each case. The lower melting derivative was found to contain about 15% N_2. The compounds which were evidently the result of deep-seated reactions, involving not only hydrolysis, but probably oxidation, were not identified because of the limited amount of material.

Action of Sodium Benzylacetoacetic Ester on Phenyl Mustard Oil.—Five grams of benzylacetoacetic ethyl ester were converted into the sodium derivative in ether and treated with 3.06 g. of the mustard oil. The mixture was refluxed for twelve hours without any change, so the ether was evaporated off and replaced with toluene. Two hours' boiling with the latter resulted in the formation of a yellow crystalline mass which was separated, dissolved in ice water and extracted with ether. The cold solution was then added dropwise, with stirring, to hydrochloric acid well diluted and cooled with ice. A bulky, yellow precipitate formed which immediately changed and coagulated to an orange-colored pasty, ball, which was separated, digested with warm alcohol and filtered while warm. The residue was washed well with cold alcohol and dried in an oven at 100°. The yield of purified product was very poor.

0.2 g. subst. gave 10.4 cc. N_2 at 17° and 760 mm.

Calc. for $(C_{15}H_{15}NS)_x$: N, 5.8. Found: N, 6.0.

The new substance as prepared consisted of microscopic flattened bars, yellow in color. It is nearly insoluble in alcohol, benzene, sodium hydroxide solution and hydrochloric acid. It melts at 222–223° with decomposition. The inert character of the substance, especially toward alkali, and its high melting point indicated the formation of a polymer; hence it was called bis-benzylthioacetanilide, $CH_2(CSNHC_6H_5)CH_2C_6H_5$, although the molecular weight was not determined or the structure.

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