

p-Bromophenacyl Esters.

M. p. ° C.		M. p. ° C.	
Acetate.....	85.0	Laevulinate.....	84.0
Aconitate.....	186.0	Margarate.....	78.2
Anisate.....	152.0	Palmitate.....	81.5
Benzoate.....	119.0	Phenyl-acetate.....	89.0
Butyrate.....	63.2	Propionate.....	59.0
Iso-butyrate.....	76.8	Pyromucate.....	138.5
Caprate.....	66.0	Salicylate.....	140.0
Caproate.....	71.6	Sebacate.....	147.0
Caprylate.....	65.5	Sorbate.....	129.0
Cinnamate.....	145.6	Stearate.....	78.5
Citrate.....	148.0	Succinate.....	211.0
Erucate.....	61.0	Thiocyanate.....	146.5
Ethyl-glycolate.....	104.8	<i>o</i> -Toluate.....	56.9
Glycolate.....	138.0	<i>m</i> -Toluate.....	108.0
Hippurate.....	151.0	<i>p</i> -Toluate.....	153.0
Hydrocinnamate.....	104.0	Tricarallylate.....	138.2
Lactate.....	112.8	Valerate.....	63.6
		Isovalerate.....	68.0

p-Iodophenacyl Esters.

M. p. ° C.		M. p. ° C.	
Acetate.....	114.0	Erucate.....	73.8
Benzoate.....	126.5	Lactate.....	139.8
Butyrate.....	81.4	Margarate.....	88.8
Iso-butyrate.....	109.2	Palmitate.....	90.0
Caprate.....	80.0	Propionate.....	94.9
Caproate.....	81.5	Stearate.....	90.5
Caprylate.....	77.0	Valerate.....	78.6
Iso-valerate.....	78.8		

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[CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF TUFTS COLLEGE.]

THE ADDITION OF 1,3-DIKETONES TO ISOTHIOCYANATES.
I. ACETYLACETONE AND CERTAIN ARYL
ISOTHIOCYANATES.

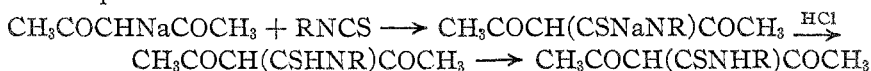
BY DAVID E. WORRALL.

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The β -diketones are characterized by several reactions that make them of particular value for synthetic purposes. They react with hydroxylamine and with phenylhydrazine to form mono-substituted derivatives; but, through the loss of a molecule of water, these rearrange to form isoxazols and pyrazols, reactions that illustrate the ease with which 5-membered ring compounds may be closed. The presence of an acidic methylene group makes possible the formation of metal derivatives; hence these diketones are capable of transformations similar to those so well known with malonic ester.

Phenyl mustard oil reacts readily with sodium acetoacetic and malonic esters to form thio-anilides.¹ This reaction was shown later to be general for aryl mustard oils.² It has now been found that the addition takes place just as readily with the sodium derivative of 1,3-diketones and probably is a general reaction for similar compounds containing hydrogen replaceable by a metal. This will be investigated in order to find the scope and limits of the reaction. Work is in progress with other diketones and esters.

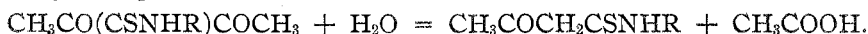
Sodium acetylacetone was found to react at room temperature with phenyl-, with the 3 tolyl- and with *p*-bromophenyl isocyanates. The final product in each case was a thio-anilide. The transformations may be interpreted as follows:



The derivatives of phenyl isothiocyanate in which the substituents were in the *para* position were found to be slightly more reactive with sodium acetylacetone than phenyl iso-thiocyanate. The nature of the substituent in the 2 cases investigated was of little, if any, significance, since *p*-bromo- and *p*-methylphenyl-isothiocyanates were added to sodium acetylacetone with equal ease, as near as could be judged. The position of the substituent, however, was of decided influence and both *o*- and *m*-tolyl-isothiocyanates reacted much more slowly with the diketone.

Finely divided metallic sodium was used to prepare sodium acetylacetone, in order to avoid the use of alcohol because of the possibility of urethane formation with the isothiocyanate. A varying but small amount of unchanged sodium was always present before the addition of water. While this undoubtedly cut down the yield somewhat it had no other effect. In favorable cases the yield of crude product was about 80% of the calculated amount, occasionally much less, of which 20% was lost in purifying the substance by recrystallization.

The resulting thio-anilides dissolved easily in dil. caustic alkali solution and, on neutralization with acid, new substances, the result of hydrolysis, separated,



The 2 series of anilides reacted very readily with organic bases such as phenylhydrazine and hydroxylamine; the point of attack was the sulfur atom. The same product was formed from the 2 corresponding anilides in each case. Thus thio-diaceto-acetyl anilide and thio-aceto-acetyl anilide gave rise to the same substance with phenylhydrazine, namely

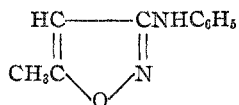
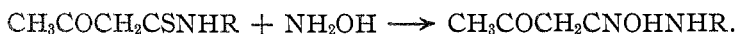
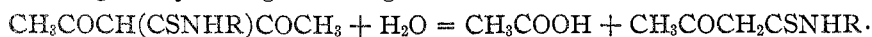
¹ Michael, *J. prakt. Chem.*, [2] 35, 450 (1887); [2] 60, 286 (1889); Ruheman, *J. Chem. Soc.*, 93, 621 (1908).

² Worrall, *THIS JOURNAL*, 40, 415 (1918).

the hydrazone of thioformanilide. Reduction as well as condensation must have taken place.



The action of hydroxylamine appeared to result in the formation of an isoxazol. Thio-diaceto-acetyl anilide and thio-aceto-acetyl anilide formed the same product, showing the ease with which the former is hydrolyzed. The resulting anilide then condensed with hydroxylamine, with the elimination of hydrogen sulfide. Reduction did not take place in this case and as the resulting oxime contained a carbonyl group in the β -position to the oxime radical, conditions were favorable for anhydride formation, resulting finally through rearrangement, in an isoxazol.



This compound is insoluble in alkali, soluble in conc. hydrochloric acid, in which it is unchanged by short heating, and does not appear to react with acetyl chloride.

Experimental.

Thio-diaceto-acetyl Anilide, $\text{CH}_3\text{COCH}(\text{CSNHC}_6\text{H}_5)\text{COCH}_3$.—Ten g. of acetylacetone was converted into the sodium derivative by addition to 2.3 g. of sodium suspended in 100 cc. of ether. A vigorous reaction took place at first, but was not completed for some time. Accordingly, the mixture was kept at room temperature for at least 24 hours before it was used. The molecular equivalent of phenyl-isothiocyanate was added. The ether became colored yellow in a few minutes, while the white powdery sodium acetylacetone slowly changed into a heavy yellow granular solid, somewhat pasty when it separated out on the sides of the container. After several days the mixture was treated with ice-water, the water layer separated and poured into a large volume of cold dil. hydrochloric acid. The turbid solution deposited a voluminous crystalline precipitate in a few minutes. This was separated, crystallized twice from benzene and air-dried at 100° .

Calc. for $\text{C}_{12}\text{H}_{13}\text{ONS}$: N, 6.0; S, 13.6. Found: N, 6.8; S, 13.4.

The sulfur was determined by treating a weighed amount of the substance with an excess of phenylhydrazine. The mixture was warmed gently to complete the reaction. The hydrogen sulfide evolved in an atmosphere of hydrogen was forced to bubble through ammoniacal cadmium sulfate solution and the resulting cadmium sulfide was separated and heated to constant weight at 110° in a Gooch crucible. This pro-

cedure was necessary, as it was found to be extremely difficult to oxidize this thio-anilide completely with nitric acid. A vigorous reaction took place at room temperature, but the resulting yellow substance was not entirely decomposed after 3 hours heating in a sealed tube at 200–250°. This compound was not identified, but was found to be free from nitrogen, although it contained sulfur. This work with nitric acid was done by Mr. Lee Smith, of Harvard University, in attempts to determine sulfur by the Carius method.

Thio-diaceto-acetyl anilide is readily soluble in alcohol, acetone, ammonium hydroxide and conc. acids. It is less soluble in benzene and insoluble in petroleum ether and water. It crystallizes from benzene in slender pale yellow needles, which melt at 107–108°. It is unstable toward alkaline reagents, more stable with the mineral acids, but easily decomposed by the latter if heated. Bromine is readily absorbed with subsequent evolution of hydrogen bromide.

The thio-anilide is completely decomposed by hot hydrochloric acid. Hydrogen sulfide is evolved, acetic acid formed, and also aniline hydrochloride. Potassium permanganate is easily reduced in the cold with the formation of isonitrile, recognized by its characteristic odor.

Thio-aceto-acetyl Anilide, $\text{CH}_3\text{COCH}_2\text{CSNHC}_6\text{H}_5$.—Two g. of thio-diaceto-acetyl anilide was dissolved in dil. potassium hydroxide solution and kept at room temperature for a few hours. It was then cooled with ice and cautiously neutralized with cold dil. hydrochloric acid. A pale yellow oil separated. It quickly hardened to a crystalline mass and was recrystallized from alcohol diluted with water.

Calc. for $\text{C}_{10}\text{H}_{11}\text{ONS}$: N, 7.3. Found: 7.8.

It is very soluble in alcohol, benzene, ether, etc., and sparingly soluble in hot water. It is easily superfused, so the following procedure was devised as most convenient for purification. The crude product is dissolved in hot alcohol and warm water is added until a faint turbidity appears. The mixture is allowed to cool to room temperature, filtered to remove tarry material that forms, and then placed in a cold place overnight. The thioaceto-acetyl anilide separates in brilliant yellow plates, m. p. 63.5–64°. The reactions of this substance are very similar to those of the diaceto derivative, due to the ease with which the latter hydrolyzes to form acetic acid and thio-aceto-acetyl anilide.

Action of Phenylhydrazine on Thio-diaceto-acetyl Anilide.

Two g. of anilide was mixed with the molecular equivalent of phenylhydrazone. The mixture quickly became warm with an immediate evolution of hydrogen sulfide. It was heated for an hour on the steam bath and then cooled. The resulting oil hardened on standing to a stiff paste which was pressed on a clay plate and crystallized twice from benzene.

Calc. for $C_{13}H_{13}N_3$: N, 19.9. Found: 20.2.

The new substance is the phenylhydrazone of thioformanilide, $HC(NN-HC_6H_5)NHC_6H_5$. It separates from benzene-petroleum ether mixture in lustrous white plates, which are somewhat irregular, m. p. $126-127^\circ$. It may be crystallized from water. If heated for a few minutes with conc. hydrochloric acid, crystals of phenylhydrazine hydrochloride separate. These were identified by the melting point, 240° , and by treating the salt neutralized with sodium hydroxide with benzaldehyde. The oil first formed quickly reacted to form a crystalline derivative.

3-Anilino-5-methylisoxazol.—Three g. of thio-diaceto-acetyl anilide,



dissolved in alcohol, was refluxed for several hours with free hydroxylamine, prepared by neutralization of the hydrochloride with potassium carbonate. The colorless solution was then evaporated to a small volume, the precipitate crystallized from hot water and dried *in vacuo*.

Calc. for $C_{10}H_{14}ON_2$: N, 16.1. Found: 16.5.

It is soluble in the usual organic solvents except petroleum ether and may be crystallized from benzene, or a large volume of water, in slender colorless needles melting at $111-112^\circ$. It is insoluble in cold alkali, but somewhat soluble in hot sodium hydroxide solution, from which it subsequently separates unchanged. It is not decomposed by short heating with conc. hydrochloric acid, in which it is easily soluble.

Thio-diaceto-acetyl *p*-Toluide, $CH_3COCH(CSNHC_6H_4CH_3)COCH_3$.—Five g. of acetylacetone was converted into the sodium derivative and mixed with the molecular equivalent of *p*-tolyl mustard oil. At the end of 3 days the mixture was dissolved in cold water, the water layer separated and acidified with cold dil. acid. The yield was slightly over 10 g. of crude material from which 8 g. of pure substance was recovered by crystallization from benzene.

Calc. for $C_{18}H_{16}O_2NS$: N, 5.6. Found: 6.4.

The thiotoluide crystallizes from benzene in balls of pointed yellow plates that melt at $132-133^\circ$.

Thio-aceto-acetyl-*p*-toluide, $CH_3COCH_2CSNHC_6H_4CH_3$.—Two g. of thio-aceto-acetyl-*p*-toluide was dissolved in a warm solution of potassium hydroxide. After a few hours the solution was neutralized with acid. The precipitate which formed was recrystallized from dil. alcohol as pale yellow microscopic needles, melting at $68-69^\circ$.

Calc. for $C_{11}H_{13}ONS$: N, 6.8. Found: 7.2.

of sodium acetylacetone and allowed to stand for a week. The new sodium derivative was dissolved in ice-water and decomposed with cold dil. acid. A vivid yellow oil separated and slowly hardened on standing. Only about a gram of the product was obtained. It crystallized from benzene mixture in shining yellow plates, m. p. 124-125°.

Calc. for $C_{18}H_{16}O_2NS$: N, 5.6. Found: 6.1.

Thio-diaceto-acetyl-*o*-toluide, $CH_3COCH(CSNHC_6H_4CH_3)COCH_3$.— Five g. of acetylacetone was converted into the sodium derivative and kept for a week with the equivalent of *o*-tolyl isothiocyanate mixed with ether. The mixture treated in the customary manner, gave 3 g. of crude material. This was purified by use of benzene-petroleum ether. Pale yellow irregular plates were obtained, m. p. 126.5-128°.

Calc. for $C_{18}H_{16}O_2NS$: N, 5.6. Found: 6.1.

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[CONTRIBUTION FROM THE OFFICE OF PLANT PHYSIOLOGICAL AND FERMENTATION INVESTIGATIONS, BUREAU OF PLANT INDUSTRY, U. S. DEPARTMENT OF AGRICULTURE.]

THE MOSAIC DISEASE OF SPINACH AS CHARACTERIZED BY ITS NITROGEN CONSTITUENTS.¹

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Introduction.

Spinach belongs to leafy vegetables which are essentially different from what may be classed as seeds, roots, and tubers. While the latter² representing storage organs contain chiefly reserve proteins, carbohydrates and fats, and but very little active protoplasm, the former³ are made up of a large quantity of functioning cells combined with reserve food material. Whereas roots,⁴ seeds and tubers are deficient in certain inorganic elements and in the dietary essential, fat soluble vitamine A, containing at the same time proteins of low biological value, leaves are comparatively rich in inorganic elements, especially in calcium and sodium, as well as in the fat-soluble vitamine A. This is especially true of spinach⁵ (*Spinacia oleracea*), which is comparatively rich both in the fat-soluble vitamine A and in the water-soluble vitamine B, being twice as efficient as whole wheat, soy beans, dried eggs or milk solids. These important nutritive qualities of spinach make it desirable to ascertain the nature of the mosaic disease of spinach with the object in view of finding a proper remedy for the disease.

¹ Presented before the Division of Biological Chemistry at the St. Louis meeting of the American Chemical Society, April 12-17, 1920.

² McCollum, Simmonds and Parsons, *J. Biol. Chem.*, 38, 115 (1919).

³ McCollum, Simmonds and Pitz, *ibid.*, 30, 19 (1917).

⁴ *Loc. cit.*

⁵ Osborne and Mendel, *ibid.*, 37, 190 (1919).