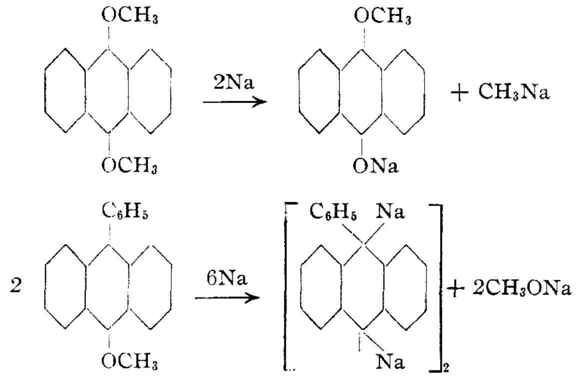
[Contribution from the School of Chemistry of the University of Minnesota]

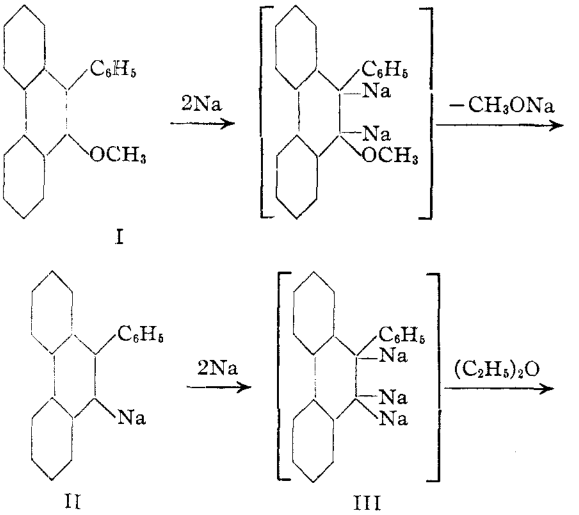
The Action of Sodium on 9-Methoxy-10-phenylphenanthrene and on 1-Diphenylene-3-phenylindene

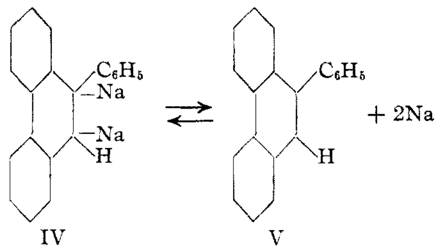
By C. Frederick Koelsch

A study of the addition of sodium to compounds which have an ether grouping directly attached to the unsaturation involved should lead to interesting data, for in the two cases of this kind which have been previously investigated, entirely unpredictable results have been obtained. While anthracene and 9-phenylanthracene simply add sodium to the 9,10 positions, their methoxylated derivatives behave as follows[1]



In the present paper it is shown that 9-methoxy-10-phenyl-phenanthrene behaves in a still different way. The reaction appears to take place in several stages which may be represented by the following formulas:





9-Methoxy-10-phenylphenanthrene is nearly insoluble in ether, but if a suspension of this substance in dry ether is shaken with 40% sodium amalgam it soon dissolves, giving a clear light brown solution. If the solution is hydrolyzed at this point, it gives only 9-phenylphenanthrene, while if it is carbonated it gives 9-phenylphenanthrene together with an approximately equal amount of 9-phenylphenanthrene-10-carboxylic acid. If, however, the amalgam is allowed to continue to react, the solution becomes deep violet. This violet solution reacts with carbon dioxide, benzaldehyde, benzoyl chloride, or methyl chlorocarbonate to give 9-phenylphenanthrene; its hydrolysis gives both this hydrocarbon and 9-phenyl-9,10-dihydrophenanthrene.

Since carbon dioxide reacts with the violet solution, as is shown by the disappearance of the color, but gives only 9-phenylphenanthrene and not an acid, the tri-sodium compound (III) cannot be present, for carbon dioxide reacting with (III) as it must[2] in converting (IV) into (V), would give (II) which has been shown to be carbonated normally. The odd sodium atom in (III) must be sufficiently active to react with the solvent, $\mathrm{RNa} + (\mathrm{C_2H_5})_2\mathrm{O} \longrightarrow \mathrm{RH} + \mathrm{C_2H_4} + \mathrm{C_2H_5ONa}$, as does sodium benzyl.[3]

That the equilibrium between (IV) and (V) + 2Na (or $\mathrm{Na_xHg}$) does exist, is evidenced by the fact that hydrolysis of the violet solution gives

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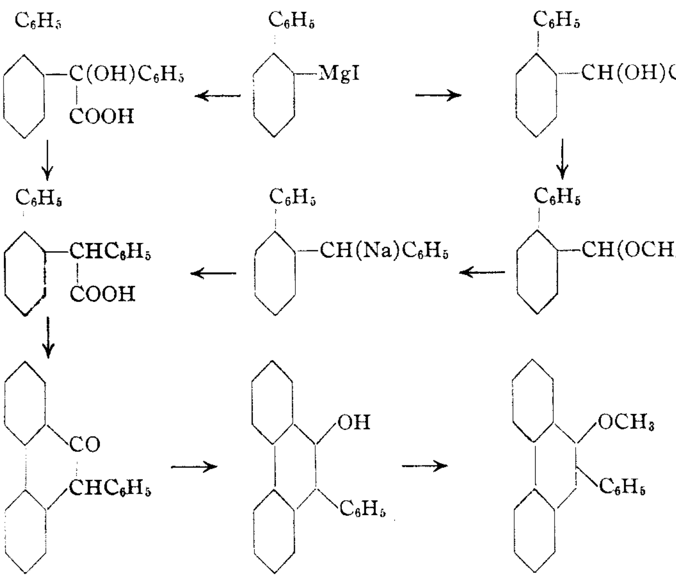
(1) Schlenk and Bergmann, *Ann.*, **464**, 36 (1928).

(2) Schlenk and Bergmann have shown [*ibid.*, **463**, 10 (1928)] that a variety of reagents remove the metal from 1,2-disodium compounds, generating a double bond; *e. g.*, $\overset{\vee}{\mathrm{C}}(\mathrm{Na})\overset{\vee}{\mathrm{C}}(\mathrm{Na}) + 2\mathrm{ClCO_2CH_3} \longrightarrow \overset{\vee}{\mathrm{C}}{=}\overset{\vee}{\mathrm{C}} + (\mathrm{CO_2CH_3})_2 + 2\mathrm{NaCl}$. It seems not unreasonable to suppose that in the present case carbon dioxide reacts analogously: $\overset{\vee}{\mathrm{C}}(\mathrm{Na})\overset{\vee}{\mathrm{C}}(\mathrm{Na}) + 2\mathrm{CO_2} \longrightarrow \overset{\vee}{\mathrm{C}}{=}\overset{\vee}{\mathrm{C}} + (\mathrm{CO_2Na})_2$.

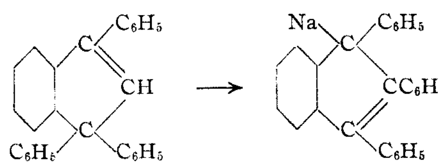
(3) Schorigin, *Ber.*, **43**, 1931 (1910); Ziegler, Colonius and Schaefer, *Ann.*, **473**, 49, note 3 (1929); Schlenk and Bergmann, *ibid.*, **464**, 21 (1928).

not only 9-phenyl-9,10-dihydrophenanthrene but also some 9-phenylphenanthrene.

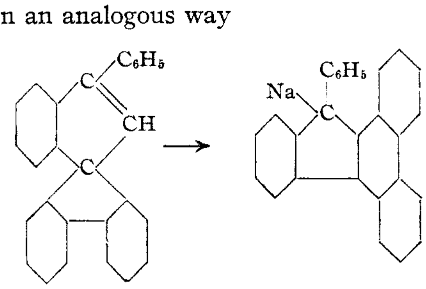
The 9-methoxy-10-phenylphenanthrene used was prepared in two ways, illustrated by the following formulas



It has been shown[4] that the action of sodium on 1,1,3-triphenylindene results in the formation of a monosodium compound, a phenyl group migrating in the reaction



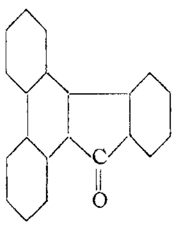
The related compound, 1-diphenylene-3-phenylindene, was recently treated with sodium,[5] and here too it was found that a monosodium compound was formed. Evidence adduced below now makes it possible to state that this reaction proceeds in an analogous way



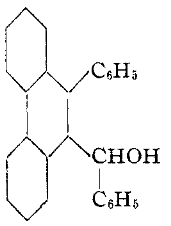
The product reacts with water to give 1,2,3,4-dibenzo-9-phenylfluorene, with carbon dioxide to give the corresponding 9-carboxylic acid, and with benzoyl chloride to give the corresponding 9-benzoyl derivative; rather remarkably, methyl benzoate does not react with the sodium compound.

Many fruitless attempts were made to establish the constitution of 1,2,3,4-dibenzo-9-phenylfluorene by degradation. The only definite results were obtained with chromic acid in acetic acid. This reagent gives an amorphous acid, a red compound, and a colorless compound $C_{27}H_{18}O_3$. Since no information of value could be obtained from the further reactions of these substances, attention was directed toward the synthesis of 1,2,3,4-dibenzo-9-phenylfluorene.

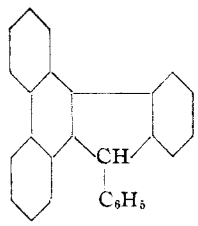
1,2,3,4-Dibenzofluorenone (VI), obtained from 9-phenylphenanthrene-10-carboxylic acid, apparently does not react normally with phenylmagnesium bromide, for the uncrystallizable reaction product does not form a halochromic salt with sulfuric acid in acetic acid, does not give a crystalline ether with methanol and sulfuric acid, and is not reduced by zinc in acetic acid. The desired synthesis is, however, realized by allowing 9-phenylphenanthryl-10-sodium to react with benzaldehyde, forming (VII), and dehydrating this carbinol with sulfuric acid in acetic acid to the hydrocarbon (VIII). This substance is identical with that obtained from 1-diphenylene-3-phenyl-indene; it reacts with sodium amalgam to give a yellow sodium compound which, when treated with benzoyl chloride, gives a benzoyl derivative identical with that obtained from the indene in a similar way.



VI



VII



VIII

Experimental

o-Phenylbenzohydrol.—To a solution of o-xenylmagnesium iodide[6] containing 4 g. of magnesium is added 16 g. of benzaldehyde in ether. The solid addition product is filtered off after one hour, washed with ether and de-

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[4] Ziegler and Crossman, *Ber.*, **62**, 1768 (1929).

[5] Koelsch, THIS JOURNAL, **55**, 3398 (1933).

[6] Clarkson and Gomberg, *ibid.*, **52**, 2884 (1930).

composed with iced ammonium chloride. The product, crystallized from ether–petroleum ether, melts at 69–70°; yield, 21 g.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.7; H, 6.1. Found: C, 87.6; H, 6.1.

On boiling this carbinol in acetic acid containing a little sulfuric acid or on treating the carbinol dissolved in ether with thionyl chloride there is obtained a quantitative yield of 9-phenylfluorene (mixed melting point).

_o_-Phenylbenzohydryl Methyl Ether.—The hydrol (19 g.) dissolved in methanol (80 ml.) containing 5% of sulfuric acid is allowed to stand at room temperature for twenty-four hours. On scratching, the solution deposits 14 g. of the ether. From the mother liquor an additional 1.4 g. may be obtained. The compound forms white needles that melt at 72–73°.

Anal. Calcd. for $C_{20}H_{18}O$: C, 87.6; H, 6.6. Found: C, 87.5; H, 6.6.

Cleavage of _o_-Phenylbenzohydryl Methyl Ether by Sodium.—A solution of 12 g. of the ether in 150 ml. of ether is shaken under nitrogen for four days with an excess of powdered sodium. The red organo-alkali compound is carbonated in the usual way, and the resulting acid is crystallized from dilute acetic acid. There is obtained 7.5–8 g. of phenyl-*o*-xenylacetic acid, melting at 171–173°.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.2; H, 5.6. Found: C, 82.8; H, 6.0.

_o_-Phenylbenzilic Acid.—To a solution of *o*-xenylmagnesium iodide containing 2.5 g. of magnesium is added 18 g. of ethyl benzoylformate dissolved in ether. The mixture is refluxed for one hour, allowed to stand for ten hours, and decomposed with dilute sulfuric acid. The ether layer is removed, the solvent is distilled, and the residue is boiled for ten minutes with 100 ml. of 10% alcoholic potash. The resulting solution is poured into water, filtered and acidified. The precipitate is crystallized from acetic acid giving 16.5 g. of white needles that melt at 189–191° with decomposition. From the mother liquor an additional 3.5 g. of the acid may be obtained.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.9; H, 5.3. Found: C, 78.6; H, 5.4.

o-Phenylbenzilic acid is readily oxidized by chromic acid in acetic acid giving as the sole product *o*-phenylbenzophenone which melts at 87–89° (literature[7] 90°).

Reduction of _o_-Phenylbenzilic Acid.—A mixture of 36 g. of *o*-phenylbenzilic acid, 2.5 g. of iodine, 6 g. of red phosphorus and 150 ml. of acetic acid is boiled for four hours, filtered, and poured into water. The product is crystallized from dilute acetic acid, giving 30 g. of phenyl-*o*-xenylacetic acid; from the mother liquor an additional 4 g. of the substance may be obtained. The product melts at 171–173° alone or mixed with the acid obtained from phenyl-*o*-xenylsodium.

9-Phenylphenanthrol-10.—To 31 g. of phenyl-*o*-xenylacetic acid dissolved in 300 ml. of benzene is added 24 g. of phosphorus pentachloride, and the solution is boiled as long as hydrogen chloride is evolved. Aluminum chloride (16 g.) is then added in portions and with stirring, after which the mixture is refluxed for fifteen minutes. The solution is cooled and treated with iced hydrochloric acid and the benzene is removed with steam. The solid residue is distilled under reduced pressure and crystallized from acetic acid, giving 21 g. of the phenol; the mother liquor yields an additional 2.1 g. of the substance.

Anal. Calcd. for $C_{20}H_{14}O$: C, 88.8; H, 5.2. Found: C, 88.7; H, 5.7.

9-Phenylphenanthrol crystallizes in flat needles that melt at 142–143°; it imparts a yellow color to aqueous sodium hydroxide, but is little soluble; it is readily soluble, however, in 20% sodium hydroxide to which has been added an equal volume of methanol. The phenol is readily attacked by aqueous permanganate and by chromic acid in acetic acid, but no crystalline oxidation products could be obtained.

The acetate obtained by the action of cold acetic anhydride containing a little sulfuric acid forms a white crystalline powder from acetone–petroleum ether; it melts at 153–155°.

Anal. Calcd. for $C_{22}H_{16}O_2$: C, 84.5; H, 5.1. Found: C, 84.4; H, 5.6.

The benzoate prepared by the Schotten–Baumann reaction and crystallized from benzene–petroleum ether forms white needles that melt at 179–180°.

Anal. Calcd. for $C_{27}H_{18}O_2$: C, 86.6; H, 4.8. Found: C, 86.7; H, 4.9.

The picrate crystallized from alcohol forms orange-red needles that melt at 135°.

Anal. Calcd. for $C_{26}H_{18}O_8N_3$: C, 62.5; H, 3.4. Found: C, 62.4; H, 3.6.

9-Methoxy-10-phenylphenanthrene.—Adding methyl sulfate to a solution of sodium hydroxide and the phenol in methanol gives less than 10% of the ether. The following procedure gives a quantitative yield. The phenol (19 g.) and 20 ml. of methyl sulfate are dissolved in 300 ml. of methanol. While this solution is being gently refluxed, a solution of 20 g. of sodium hydroxide in 60 ml. of water is added dropwise, the ether crystallizing out immediately. It is recrystallized from acetic acid, when it forms long colorless needles that melt at 189–190°.

Anal. Calcd. for $C_{21}H_{16}O$: C, 88.7; H, 5.6. Found: C, 88.5; H, 5.7.

The Monosodium Compound (II).—A suspension of 0.5 g. of 9-methoxy-10-phenylphenanthrene in 25 ml. of ether is sealed under nitrogen with 1-2 ml. of 40% sodium amalgam. The reaction starts after about ten minutes of shaking. When a violet color appears around the amalgam, soon after the methyl ether has dissolved, shaking is stopped, and the amalgam is frozen and removed.

The clear yellow-brown solution is decolorized by alcohol. Removal of the ether leaves 0.45 g. of 9-phenylphenanthrene which melts above 100° before recrystallization. Crystallization from acetic acid gives the pure hydrocarbon as white plates that melt at 105–106°.

Anal. Calcd. for $C_{20}H_{14}$: C, 94.5; H, 5.5. Found: C, 94.3; H, 5.5. *Mol. wt.* Calcd.: 254. Found (Rast): 290.

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(7) Schlenk, Bergmann and Knorr, *Ann.*, **464**, 33 (1928).

The picrate crystallizes from alcohol in orange-red needles that melt at 115°.

Anal. Calcd. for $C_{26}H_{17}O_7N_3$: C, 64.6; H, 3.5. Found: C, 65.8; H, 4.7.

9-Phenylphenanthrene evolves no hydrogen sulfide when heated at 270° with sulfur, and it may be recovered unchanged after this treatment. Its solution in acetic acid slowly decolorizes an equivalent amount of bromine; the product, **9-bromo-10-phenylphenanthrene,** washed with petroleum ether and crystallized from acetic acid forms colorless prisms that melt at 108–110°.

Anal. Calcd. for $C_{20}H_{13}Br$: C, 72.0; H, 3.9. Found: C, 71.6; H, 4.3.

9-Phenylphenanthrene-10-carboxylic Acid.—A solution of the monosodium compound prepared from 5 g. of the methyl ether is carbonated in the usual way. The acidic product, crystallized from acetic acid, forms colorless plates that melt at 185–187° and are easily soluble in aqueous soda; yield, 1.8 g.

Anal. Calcd. for $C_{21}H_{14}O_2$: C, 84.5; H, 4.7. Found: C, 84.4; H, 4.8.

There is also obtained 2.2 g. of 9-phenylphenanthrene.

1,2,3,4 - Dibenzofluorenone (VI).—9 - Phenylphenanthrene-10-carboxylic acid (1.3 g.) is refluxed for four hours with 2 ml. of thionyl chloride dissolved in carbon tetrachloride.[8] The solution is then poured into water, the carbon tetrachloride is evaporated, and the crystalline residue is distilled under reduced pressure. The product (0.8 g.) crystallizes from acetic acid in the form of orange-red needles that melt at 186–187°.

Anal. Calcd. for $C_{21}H_{12}O$: C, 90.0; H, 4.3. Found: C, 90.0; H, 4.4.

The Disodium Compound (IV).—If the solution of the monosodium compound is allowed to remain in contact with the amalgam, it soon becomes deep violet. At the end of eight hours shaking, gas is liberated when the tube is opened. The solution is decolorized by carbon dioxide, but the only product obtained is 9-phenylphenanthrene (0.45 g.). Similar results are obtained with methyl chlorocarbonate, benzaldehyde and benzoyl chloride. Hydrolysis of the violet solution from 0.5 g. of the ether gives 0.15 g. of 9-phenylphenanthrene and 0.3 g. of a colorless oil. This oil evolves hydrogen sulfide when heated at 250° with sulfur and is converted into 9-phenylphenanthrene. The product obtained by reducing 9-phenylphenanthrene with sodium in amyl alcohol is likewise an oil; it does not form a picrate.

Sodium amalgam reacts rapidly with an ether solution of 9-phenylphenanthrene to give a violet solution apparently identical with that obtained from the methoxy compound.

9-(α-Hydroxybenzyl-)-10-phenylphenanthrene (VII) and its Dehydration to 1,2,3,4-Dibenzo-9-phenylfluorene (VIII).—To a solution of 9-phenylphenanthryl-10-sodium from 0.5 g. of 9-methoxy-10-phenylphenanthrene is added 1 ml. of freshly purified benzaldehyde. The solution is poured into water and the excess benzaldehyde is removed with steam. The product cannot be obtained crystalline. It is dissolved in acetic acid (5 ml.), 2 drops of concd. sulfuric acid is added, and the solution is boiled. The hydrocarbon (VIII) separates immediately from the hot solution. On recrystallization from xylene it forms white needles that melt at 210–211° alone or mixed with the hydrocarbon from 1-diphenylene-3-phenylindene; yield, 0.2 g.

1,2,3,4-Dibenzo-9-benzoyl-9-phenylfluorene. (a) **From 1-Diphenylene-3-phenylindene.**—A solution of the yellow sodium compound from 2 g. of the indene is decolorized immediately by an excess of benzoyl chloride; the product, crystallized from xylene, forms white prisms that melt at 228–229°.

Anal. Calcd. for $C_{34}H_{22}O$: C, 91.3; H, 4.9. Found: C, 91.2; H, 4.9.

(b) **From 1,2,3,4-Dibenzo-9-phenylfluorene.**—The hydrocarbon (0.1 g.) suspended in 10 ml. of ether rapidly dissolves when shaken with an excess of 40% sodium amalgam. The yellow solution formed is decolorized by benzoyl chloride, and the product (0.06 g.) is crystallized from xylene. It forms white prisms that melt at 228–229° alone or mixed with the substance described in the preceding paragraph.

Experiments on the Degradation of 1,2,3,4-Dibenzo-9-phenylfluorene Obtained from 1-Diphenylene-3-phenylindene.—To a boiling suspension of 7.7 g. of the hydrocarbon in 250 ml. of acetic acid is added slowly a dilute acetic acid solution of chromic acid (6 g.). The solution is poured into water and the precipitate is taken up in ether. Dilute sodium carbonate removes a resinous acid; the neutral products remaining in the ether are separated by fractional crystallization from benzene–petroleum ether. One product crystallizes from acetic acid in orange needles that melt at 207–208°; yield, 0.1 g. (Found: C, 94.2, 94.0; H, 5.2, 5.1.)

The other product separates from acetic acid in colorless prisms that melt at 188–189°; yield, 2.5 g.

Anal. Calcd. for $C_{27}H_{18}O_3$: C, 83.0; H, 4.6. Found: C, 82.8; H, 4.7.

The colorless product gives a yellow color with cold sulfuric acid; it reacts on long boiling with hydroxylamine in alcohol to give a very poor yield (*ca.* 5%) of a substance that melts at 218–220° with decomposition. On boiling with hydriodic acid in acetic acid, $C_{27}H_{18}O_3$ is converted into an insoluble substance containing iodine; recrystallized from cold nitrobenzene–petroleum ether this substance forms red-brown needles that darken at 125° and melt sharply at 185–187°. (Found: C, 45.0; H, 2.8.)

The substance $C_{27}H_{18}O_3$ dissolves in boiling 5% alcoholic sodium hydroxide to give a brown solution. On adding water and dilute hydrochloric acid, a substance is obtained which forms yellow prisms from benzene that melt at 184–186°; it cannot be recrystallized from acetic acid, separating from this solvent as a red oil which, however, is reconverted into the 184–186° substance by solution in benzene. This substance forms a bright red difficultly soluble sodium salt with alcoholic sodium hydroxide and gives a bright red color with cold sulfuric acid.

Anal. Calcd. for $C_{27}H_{16}O_2$: C, 87.1; H, 4.3. Found: C, 87.2; H, 5.2.

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(8) Koelsch, THIS JOURNAL, **54**, 2487 (1932).

Summary

Sodium reacts with 9-methoxy-10-phenylphenanthrene in ether to give 9-phenylphenanthryl-10-sodium. This can react further with sodium to give a compound which appears to be the disodium addition product of 9-phenylphenanthrene.

1 - Diphenylene - 3 - phenylindene is converted by sodium into 1,2,3,4-dibenzo-9-phenylfluorene-9-sodium.

MINNEAPOLIS, MINN. RECEIVED NOVEMBER 8, 1933

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

The Synthesis of Thiazole Barbituric Acids. XIII

BY FLORENCE E. HOOPER[1] AND TREAT B. JOHNSON

Since Fischer and von Mering's discovery in 1903 of the hypnotic properties of 5,5-diethylbarbituric acid, great interest has been shown in the preparation and study of other 5,5 derivatives of this pyrimidine. With few exceptions,[2] however, little attention has been devoted to such derivatives in which one of the substituent groups in position 5 includes an heterocyclic configuration. In view of the prevalence of such groups in many physiologically active substances the preparation of heterocyclic substituted derivatives of barbituric acid would seem to be of considerable interest. This paper reports the synthesis of 5-ethyl-5-(2-methylthiazole-4-methyl)- and 5-ethyl-5-(2-phenylthiazole-4-methyl)-barbituric acids. A pharmacological investigation of these compounds is now in progress.

Both syntheses were readily accomplished by the condensation of the required substituted malonic esters with urea. The necessary esters were prepared by alkylation of diethyl ethylmalonate with 2-methyl-4-chloromethyl- and 2-phenyl-4-chloromethyl-thiazoles.

Experimental Part

$ClCH_2C{=}CHSC(CH_3){=}N$, **2-Methyl-4-chloromethylthiazole (I)**, was prepared according to the method of Hooper and Johnson.[3]

$(C_2H_5OOC)_2C(C_2H_5)CH_2C{=}CHSC(CH_3){=}N$, **Diethyl ethyl-(2-methylthiazole-4-methyl)-malonate (II)** was prepared from diethyl ethylmalonate and I according to the usual procedure for malonic ester syntheses.[4] The product was a colorless odorless liquid, b. p. 168–174° at 4–5 mm.; yield 59%.

Anal. Calcd. for $C_{14}H_{21}O_4NS$: N, 4.68. Found: N, 4.60.

$CONHCONHCOC(C_2H_5)CH_2C{=}CHSC(CH_3){=}N$, **5-Ethyl-5-(2-methylthiazole-4-methyl)-barbituric Acid (III).**—Compound II was condensed with urea according to the method recommended by Dox and Yoder[5] for the preparation of 5-alkyl-5-benzylbarbituric acids. Upon acidification of the reaction mixture with hydrochloric acid, the desired product precipitated with the sodium chloride. The precipitate was extracted with water, dried and recrystallized from alcohol containing a little benzene. The product III was obtained in long slender needles, m. p. 264–265°; yield 63%.

Anal. Calcd. for $C_{11}H_{15}O_3N_3S$: N, 15.73. Found: N, 15.35, 15.45.

$ClCH_2C{=}CHSC(C_6H_5){=}N$, **2-Phenyl-4-chloromethylthiazole (IV).**—Efforts to prepare this thiazole halide by heating equimolecular portions of *sym*-dichloroacetone and thiobenzamide in alcohol resulted in yields far below that reported by Suter and Johnson.[6] The following procedure, however, consistently gave total yields of 75% or more. The hydrochloride, $ClCH_2COCH_2SC(C_6H_5){=}NH\cdot HCl$, was prepared by the reaction of equimolecular portions of *sym*-dichloroacetone and thiobenzamide in acetone solution,[3] 50 g. of the hydrochloride was suspended in a liter of acetone containing 40 cc. of concentrated hydrochloric acid and refluxed on the steam-bath until a clear solution was obtained. On cooling, a copious precipitate of the thiazole hydrochloride, $ClCH_2C{=}CHSC(C_6H_5){=}N\cdot HCl$, crystallized out in lustrous plates. An additional quantity of the hydrochloride was obtained as a sirup on concentration of the filtrate. On decomposition with aqueous sodium bicarbonate the hydrochloride gave a product identical with the 2-phenyl-4-chloromethyl-thiazole reported by Suter and Johnson.

$(C_2H_5OOC)_2C(C_2H_5)CH_2C{=}CHSC(C_6H_5){=}N$, **Diethyl ethyl-(2-phenylthiazole-4-methyl)-malonate (V)** was prepared from diethyl ethylmalonate, and IV according to the usual procedure for malonic ester syntheses.[4] The product was a pale yellow odorless oil, b. p. 208–211° at 4–5 mm.; yield 50%.

Anal. Calcd. for $C_{19}H_{23}O_4NS$: N, 3.88. Found: N, 3.72, 3.90.

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[1] Metz Research Fellow in Organic Chemistry, 1932–1933.

[2] Taggart and Richter, THIS JOURNAL, **55**, 1110 (1933).

[3] Hooper and Johnson, *ibid.*, **56**, 470 (1934).

[4] Adams and Kamm, "Organic Syntheses," John Wiley and Sons, New York, 1933, Coll. Vol. 1, p. 245.

[5] Dox and Yoder, THIS JOURNAL, **44**, 1141 (1922).

[6] Suter and Johnson, *Rec. trav. chim.*, **49**, 1066 (1930).