

[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF THE OAK RIDGE NATIONAL LABORATORY]

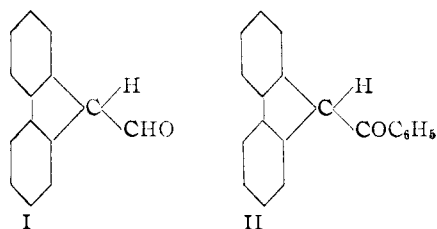
**The Displacement of the Benzoyl Group from Phenyl 9-Fluorenyl Ketone<sup>1</sup>**

BY JOHN G. BURR, JR.

The action of formalin solution upon phenyl 9-fluorenyl ketone produces 9-methylenefluorene in strong alkaline solution and 9-benzoyl-9-fluorenemethanol in weaker alkali. The existence of an equilibrium between 9-benzoyl-9-fluorenemethanol, phenyl 9-fluorenyl ketone and formaldehyde has been strongly suggested by tracer studies with C<sup>14</sup>. 9-Benzoyl-9-fluorenemethanol gives 9-methylenefluorene in alkaline formaldehyde, and thus is the probable intermediate in the formation of 9-methylenefluorene from phenyl 9-fluorenyl ketone.

**Introduction**

A consideration of the mechanism which has been proposed<sup>2</sup> to explain the displacement of the formyl group from 9-fluorencarbal<sup>3</sup> (I) and formyldeoxybenzoin<sup>2</sup> by alkaline formaldehyde suggests that carbonyl substituents other than formyl might be similarly replaced. This has now been demonstrated with phenyl 9-fluorenyl ketone (II).



When a solution of this ketone in a mixture of alcohol and 50% aqueous potassium hydroxide was treated at room temperature with a large excess of 37% formalin solution, the precipitation of 9-methylenefluorene (V), in 97% yield was complete within 15 minutes. The product was identified as 9-methylenefluorene by conversion to its well-characterized dibromide.<sup>4</sup> If the reaction was carried out at steam-bath temperature only polymeric 9-methylenefluorene was obtained.

If the alkaline solution of benzoylfluorene (II) was diluted and neutralized until the ketone just began to precipitate, or if the aqueous enolate solution obtained during the preparation of 9-benzoylfluorene was employed directly, treatment with formalin solution resulted in the precipitation of a product melting at 123–124° which had the empirical composition of 9-benzoyl-9-fluorenemethanol (III). This material was shown by mixture melting points and infrared spectra comparison to be neither benzoylfluorene or fluorenemethanol.

When III was placed in alkaline formalin solution, a transient color of benzoylfluorene enolate ion appeared. As the color faded, 9-methylenefluorene precipitated. Treatment of III with alcoholic potassium hydroxide solution resulted in regeneration of benzoylfluorene (II); and even the attempt to prepare acetyl and benzoyl esters of III in pyridine solution resulted only in the recovery of benzoylfluorene (II). Oximation in sodium carbonate solution gave the oxime of benzoylfluorene (II).

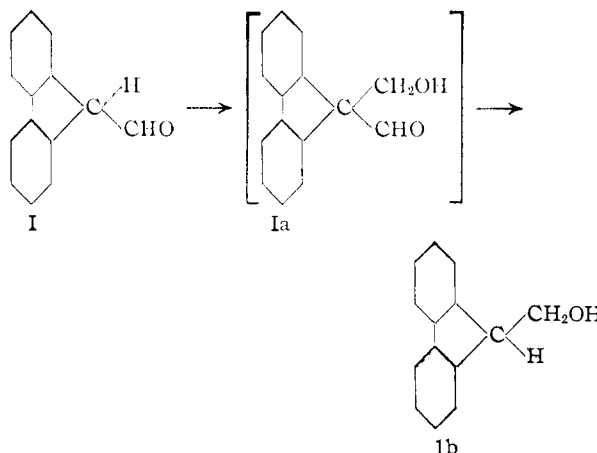
These indications of an equilibrium between 9-

benzoyl-9-fluorenemethanol (III), benzoylfluorene (II) and formaldehyde were greatly strengthened by placing a weighed amount of the benzoylfluorenemethanol (III) in alkaline 10% formaldehyde-C<sup>14</sup> solution containing a known amount of formaldehyde. The methylenefluorene so obtained (assayed as the dibromo derivative) and the formaldehyde recovered (assayed as the dimedon derivative) had specific activities which were equal and in excellent agreement with the calculated value for complete equilibrium (eq. 1).

The existence of an equilibrium between II, III and formaldehyde would not be surprising since other reversible aldol condensations are known.<sup>5</sup> This equilibrium must be established very rapidly since although the ensuing cleavage step (eq. 3) takes place completely within a few minutes, the resulting 9-methylenefluorene contains the equilibrium (eq. 1) concentration of C<sup>14</sup>.

The reaction of benzoylfluorene with alkaline formaldehyde offers several contrasts to the corresponding reaction of 9-fluorencarbal.<sup>3</sup> In the first place, the final product, in solutions of high alkaline concentration, is methylenefluorene rather than fluorenemethanol (Ib). In explanation of this, it has now been observed that 9-fluorenemethanol is dehydrated by alcoholic alkali of similar strength to 9-methylenefluorene (isolated as the polymer); and that 9-fluorencarbal in formalin solutions of high alkaline concentration also gives 9-methylenefluorene instead of 9-fluorenemethanol.

Secondly, in alkaline solutions of strength corresponding to those used with fluorencarbal<sup>3</sup> the product isolated was again not fluorenemethanol (Ib) but the intermediate product 9-benzoyl-9-fluorenemethanol (III).



(1) This document is based upon work performed under Contract Number W-7405, eng. 26 for the Atomic Energy Commission at the Oak Ridge National Laboratory.

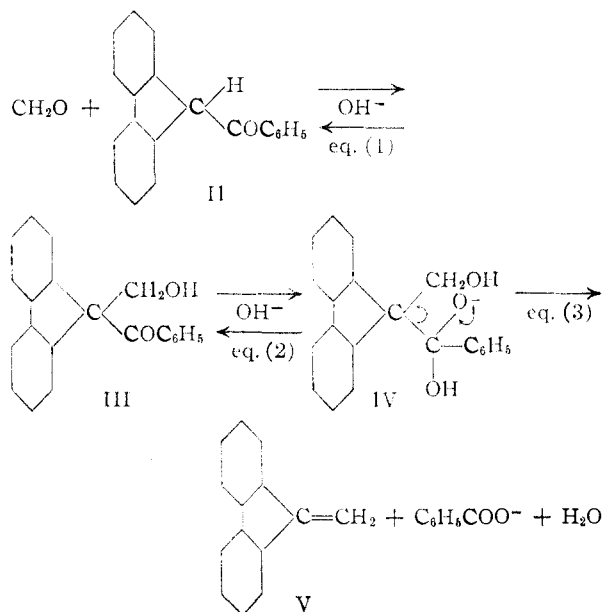
(2) J. G. Burr, Jr., *THIS JOURNAL*, **73**, 5170 (1951).

(3) J. G. Burr, Jr., *ibid.*, **73**, 823 (1951).

(4) H. Wieland, F. Reindel and J. Ferrer, *Ber.*, **55**, 3317 (1922).

(5) M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Clarendon Press, Oxford, 1949, p. 125.

The mechanism previously proposed for this type of reaction<sup>2</sup> postulated an intermediate corresponding to III. In the case of formylfluorene<sup>3</sup> (I, and Ia) and formyldeoxybenzoin this intermediate was not isolated, nor was any other specific evidence for its existence obtained. Thus, the isolation in this case of 9-benzoyl-9-fluorene-methanol (III), which is the postulated intermediate, and its facile conversion to 9-methylene-fluorene strengthens the case for this mechanism.



Also the ready isolation of the intermediate (III) shows that the substitution of a phenyl group for the aldehyde hydrogen (I *vs.* II) has exerted a decided influence upon the relative equilibria and rates of at least steps (2) and (3). Thus, if this reaction is comparable in the nature of the intermediate steps with the hydrolysis of benzoate esters (as seems reasonable from a consideration of the above mechanism), then a rate study of the reaction using variously substituted benzoylfluorenes should give evidence bearing upon the validity of the mechanism.

### Experimental<sup>6</sup>

**Phenyl 9-Fluorenyl Ketone (II).**—The procedure of Werner<sup>7</sup> gave this product in 15% yield which is in accord with the experience of others<sup>8</sup> using this method. Several attempts were made to prepare this compound in ether or benzene solution using sodium methoxide (which gave no product), and with sodium hydride (which gave an 18% yield). Finally, the action of potassium metal<sup>9</sup> gave a 64% yield of the desired ketone as white prisms, m.p. 136–137°.

**The Reaction of Phenyl 9-Fluorenyl Ketone (II) with Alkaline Formaldehyde Solution.**—(A) The ketone (0.5 g.) dissolved rapidly in a mixture of 5 ml. of ethanol and 5 ml. of 50% aqueous potassium hydroxide. To the clear orange solution was added 5 ml. of 37% formalin. After an induction period of about one minute, the solution became turbid,

(6) All melting points were taken upon a Fisher-Johns block and are uncorrected. C-14 assays were accomplished by a wet combustion of the compounds, and ionization chamber counting of the evolved carbon dioxide on a vibrating reed electrometer. Microanalyses for carbon, hydrogen, nitrogen and halogen were done by Dr. H. W. Galbraith, Knoxville, Tennessee.

(7) A. Werner, *Ber.*, **39**, 1287 (1906).

(8) A. Fehrlé and W. Wislicenus, *ibid.*, **48**, 1320 (1915).

and an additional 2 ml. of formalin was added. In about 15 minutes the solution had become colorless and a granular white solid had precipitated. Ten ml. of water was added, and the solution stirred until all additional solid had coagulated. This solid which weighed 0.32 g. (97%), and melted at 40–50°, was dissolved in hexane, and filtered from the small amount of insoluble polymer. The filtrate absorbed bromine readily and deposited 0.40 g. of massive pale yellow prisms, melting at 141–142° (lit.<sup>4</sup> is 143° for 9-bromo-9-bromomethylfluorene). Recrystallization from hexane did not change the melting point. A mixture of this with benzoylfluorene melted at less than 125°.

*Anal.* Calcd. for  $C_{14}H_{10}Br_2$ : Br, 47.3. Found: Br, 47.1.

When the aqueous filtrate from the formylation reaction was acidified and chilled, 0.16 g. (71%) of benzoic acid crystallized, whose melting point and mixture melting point with authentic benzoic acid (m.p. 119–120°) was 119–120°.

(B) When the above reaction was carried out at steam-bath temperature, the precipitated product was an amorphous powder, very slightly soluble in benzene and hexane and insoluble in ether. It was infusible, but showed shrinkage at about 300°. These physical properties accord well with those of polymethylene-fluorene.<sup>4</sup> These same authors report 9-methylene-fluorene as polymerizing with extreme readiness, even in the dark.

**9-Benzoyl-9-fluorene-methanol (III).**—(A) A solution of 0.50 g. of 9-benzoylfluorene in a mixture of 2 ml. of ethanol and 2 ml. of 50% aqueous potassium hydroxide was diluted with 5 ml. of water and neutralized dropwise with 10% hydrochloric acid until faint permanent cloudiness resulted. The resulting solution was treated with 10 ml. of water followed by 10 ml. of 37% formalin. A yellowish gum precipitated almost immediately. Ether extraction of the gum separated about 0.1 g. of polymethylene-fluorene. The ether-soluble substance (0.45 g.) deposited from hexane 0.20 g. of colorless prisms which melted at 121–124°. Recrystallization from hexane gave 0.18 g. of prisms melting at 123–124°. Mixture melting points of this substance with benzoylfluorene (m.p. 135–136°) and with fluorene-methanol (m.p. 99–100°) showed marked depressions.

*Anal.* Calcd. for  $C_{21}H_{16}O_2$ : C, 84.0; H, 5.36. Found: C, 84.0, 84.3; H, 5.51, 5.61.

When the slightly alkaline aqueous solution of benzoylfluorene (containing 0.63 g.) obtained in the preparation of benzoylfluorene was treated directly with excess formalin, immediate precipitation of the same material was observed (0.65 g.).

(B) Oxime.—A small portion of the material (0.20 g.) was converted to the oxime in sodium carbonate solution. The product formed white needles melting, after crystallization from ethanol, at 180–182°. This proved identical (by mixture melting point) with the hitherto unknown oxime of 9-benzoylfluorene.

*Anal.* Calcd. for  $C_{20}H_{15}NO$ : C, 84.2; H, 5.29; N, 4.90. Found: C, 83.9; H, 5.23; N, 4.85.

(C) Reaction with Alkali.—Another portion of the substance (0.45 g.) was stirred with a mixture of 15 ml. of ethanol and 10 ml. of 50% aqueous potassium hydroxide (the solution was homogeneous and orange in color) for one hour, then diluted with 100 ml. of water. A small amount of orange oily precipitate was filtered off, and the filtrate acidified. The pale yellow precipitate (0.30 g.) was crystallized twice from hexane to give 0.15 g. of benzoylfluorene, whose melting point and mixture melting point with authentic benzoylfluorene (m.p. 135–136°) was 135–136°.

(D) Cleavage.—A similar amount of the material (0.45 g.) was suspended in a mixture of 5 ml. of ethanol and 5 ml. of 37% formalin. To this solution was added, 5 ml. of 50% aqueous potassium hydroxide, and then 2 ml. of formalin. A deep orange color developed immediately and swiftly faded. The flocculent precipitate which formed when worked up as above gave 0.50 g. of 9-bromo-9-bromomethylfluorene, m.p. 141–142°.

**The Reaction of 9-Benzoyl-9-fluorene-methanol with Alkaline Formaldehyde-C<sup>14</sup> Solution.**—A suspension of 0.50 g. (1.67 mmoles) of the benzoylfluorene-methanol (III) in a mixture of 5 ml. of ethanol and 7 ml. of 10% formaldehyde-C<sup>14</sup> (containing 23 mmoles of C<sup>14</sup>H<sub>2</sub>O with specific activity, as determined on the dimedon derivative, of 4.24  $\mu$ c. of C<sup>14</sup>/mmole) was stirred with 5 ml. of 50% aqueous potassium hydroxide for one-half hour. The fluffy solid which

precipitated (0.25 g.) was filtered, dissolved in hexane and treated with bromine, after filtration of the solution. On chilling, 0.15 g. of dibromide crystallized. After crystallization from hexane, this was found to contain 4.01  $\mu\text{c.}$  of  $\text{C}^{14}$ /mmole (calcd. for complete equilibrium (eq. 1), 3.96

$\mu\text{c.}$  of  $\text{C}^{14}$ /mmole). The aqueous filtrate obtained above was mixed with a saturated aqueous dimedon solution. The precipitated formaldehyde derivative was found to contain 3.99  $\mu\text{c.}$  of  $\text{C}^{14}$ /mmole.

OAK RIDGE, TENNESSEE

RECEIVED OCTOBER 5, 1951

[CONTRIBUTION FROM THE B. F. GOODRICH RESEARCH CENTER]

## Reactions of 3-Thiocyano-2-butanone. I. The Preparation of 2-Substituted-4,5-dimethylthiazoles

BY JAMES T. GREGORY AND ROGER A. MATHES

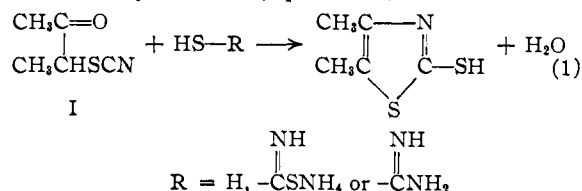
3-Thiocyano-2-butanone has been prepared and was found to react with water, hydrogen chloride, hydrogen sulfide, ammonium chloride, ammonium dithiocarbamate and thiourea to form 2-substituted-4,5-dimethylthiazoles.

Thiazoles containing substituents, other than hydrocarbon radicals, in the 2-position have been prepared from  $\alpha$ -thiocyanoketones only in a limited number of examples. 2-Aminothiazoles have been prepared by the reaction of thiocyanacetone with ammonia,<sup>1a,b</sup> ammonium thiocyanate<sup>1a</sup> and amines.<sup>1a,b</sup> The 2-hydroxy compound has been prepared by treating the  $\alpha$ -thiocyanoketones with acidic<sup>1a,2,3</sup> or basic<sup>2a</sup> reagents and the 2-chloro compound results when dry hydrogen chloride<sup>2a</sup> is used.

3-Thiocyano-2-butanone (I) was prepared by treating 3-chloro-2-butanone with aqueous sodium thiocyanate and its reactions with ammonium chloride, hydrogen sulfide, hydrogen chloride, ammonium dithiocarbamate and thiourea have been investigated.

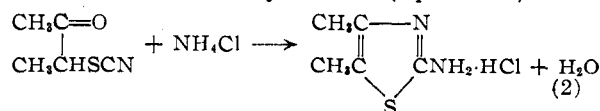
Infrared measurements<sup>4</sup> on I showed the presence of sharp peaks at 4.63 and 5.89 $\mu$  which has been reported<sup>5</sup> as characteristic of an  $\alpha$ -thiocyanoketone.

Thiourea, ammonium dithiocarbamate and hydrogen sulfide reacted with I to form 2-mercapto-4,5-dimethylthiazole (equation 1).



The reaction with hydrogen chloride gave 2-hydroxy- and 2-chloro-4,5-dimethylthiazole as co-products while with aqueous hydrogen chloride only 2-hydroxy-4,5-dimethylthiazole was isolated.

The reaction of I with aqueous ammonium chloride resulted in the formation of the hydrochloride of 2-amino-4,5-dimethylthiazole (equation 2). The



(1) (a) A. Hantzsch and J. H. Weber, *Ber.*, **20**, 3118 (1887); (b) A. Hantzsch and H. Schwaneberg, *ibid.*, **61**, 1776 (1928); (c) J. Tcherniac and T. H. Norton, *ibid.*, **16**, 345 (1883).

(2) (a) J. Tcherniac, *ibid.*, **25**, 2607 (1892); *J. Chem. Soc.*, **115**, 1071 (1919); (b) A. Hantzsch and H. Schwedler, *Ber.*, **60**, 2537 (1927).

(3) H. Andersag and K. Westphal, U. S. Patent 2,139,570.

(4) Determined by J. J. Shipman of this Laboratory.

(5) W. S. Emerson and T. M. Patrick, *J. Org. Chem.*, **13**, 722 (1948).

ultraviolet absorption spectra have been determined<sup>6</sup> and are given in Fig. 1.

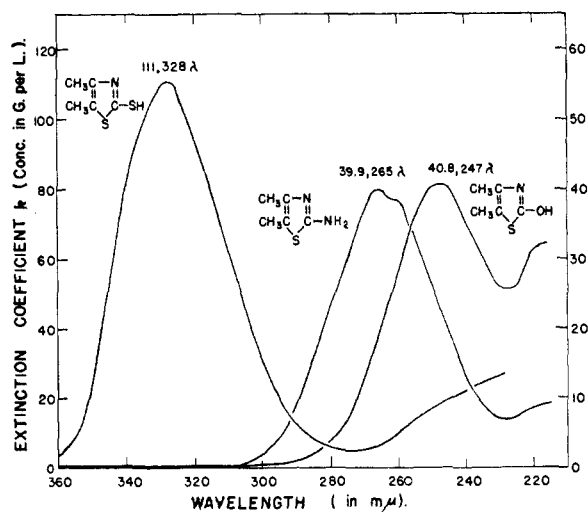


Fig. 1.

### Experimental<sup>7</sup>

**3-Thiocyano-2-butanone (I).**—3-Chloro-2-butanone (319.5 g., 3.0 moles) was added dropwise to a vigorously stirred solution of sodium thiocyanate (284 g., 3.5 moles) in 600 ml. of water over a period of 3 hours during which time the temperature was maintained at 80°. After an additional hour or stirring the mixture was cooled to 25° and the water layer withdrawn. The product (a red oil) was washed twice with water (300 ml.). The unreacted chlorobutanone and dissolved water were removed by heating the crude product to 90° at a pressure of 30 mm. The product weighed 343 g. (89%). Distillation through a short column gave a light yellow liquid, b.p. 63–68° (0.5 mm.); yield 326 g. (84.2%). By careful redistillation the product can be obtained as a water-white mobile liquid, b.p. 58–59° (0.5 mm.),  $n_D^{20}$  1.4836,  $d_4^{20}$  1.1152,  $d_4^{15}$  1.1195;  $[M_R]_D^{20}$  33.07 (found), 32.60 (calcd.).

**2-Mercapto-4,5-dimethylthiazole. By the Reaction of I and (a) Hydrogen Sulfide.**—An ethanol (200 ml.) solution of I (65 g., 0.5 mole) was placed in a stainless steel bomb (1 liter) and charged with hydrogen sulfide. The bomb was placed in a rocking mechanism and heated to 78°. The internal pressure fell from 2700 to 2100 p.s.i. The bomb was cooled and vented. The solid mush of crystals was removed and the mixture concentrated by heating the ethanolic solution. After dilution with hexane and cooling, the crystalline solid was recovered by filtration. The crude product weighed 38 g. (52.5%), m.p. 133–153°. Recrystallization from ethanol after treatment with decolorizing

(6) Determined by E. Gregg and J. Efroymson of this Laboratory.

(7) All melting points are uncorrected.