Anal. Calcd. for $C_{21}H_{28}O_7N_4S$: C, 52.5; H, 5.8. Found: C, 52.8; H, 6.0.

The product is therefore the dodecene (V) sought, the intermediate ester (IV) having suffered hydrolysis and loss of carbon dioxide.

11-(2-Thiazolyl)-undecanoic Acid (VI).—A solution of 2 g. (0.008 mole) of the dodecene (V) in 50 cc. of dry acetone was treated gradually with 4.7 g. (0.03 mole) of potassium permanganate at temperatures below 40°. The precipitate was filtered out, extracted with a 10% sodium carbonate solution, the extract concentrated and carefully acidified to obtain the maximum separation of the desired product. Inasmuch as the product was soluble in excess of acid, it was necessary to test the mother liquor with both dilute acid and dilute alkali, to ensure complete separation of the thiazole acid (VI). The oil so obtained was extracted with ether, the ether extract dried with magnesium sulfate and the ether removed. There remained a yellow viscous oil which congealed to a colorless glass in the refrigerator. Crystallization from a mixture of ethyl acetate and petroleum ether gave 1.5 g. (70% yield) of a crude product which was solid only below room temperature. Further recrystallizations yielded large colorless plates, m. p. 40–41.5°.

Anal. Calcd. for $C_{14}H_{23}O_2NS$: C, 62.4; H, 8.6. Found: C, 62.1; H, 8.6.

Picrate.—This was prepared in ether solution and was purified by crystallization from ethyl acetate. It formed yellow needles, melting with decomposition at 100–106°.

Anal. Calcd. for $C_{20}H_{26}O_9N_4S$: C, 48.2; H, 5.3. Found: C, 48.4; H, 5.5.

1-(4-Methyl-2-thiazolyl)-octene-1 (VII).—A mixture of 5.7 g. (0.05 mole) of 2,4-dimethylthiazole, 8.7 g. (0.075 mole) of *n*-heptaldehyde and 5.1 g. (0.05 mole) of acetic anhydride was heated in a sealed tube at 240–265° for thirty hours, the product of this reaction was made alkaline, extracted with ether, and the extract dried and distilled. A fraction, b. p. 180–200° (7 mm.), was collected and converted into its picrate, of which 2.4 g. was obtained. Crystallized from alcohol, the picrate formed yellow needles, m. p. 73°.

Anal. Calcd. for $C_{18}H_{22}O_7N_4S$: C, 49.3; H, 5.1. Found: C, 49.6; H, 5.1.

Summary

1. Ethyl undecylenylcyanoacetate has been prepared from undecylenyl iodide and ethyl cyanoacetate.

2. By the addition of hydrogen sulfide to the cyanogen group of this cyanoacetate, the corresponding thioamide of the ester was obtained.

3. Condensation of the thioamide with chloroacetaldehyde hydrate, in benzene solution, resulted in hydrolysis of the ester, elimination of carbon dioxide, and production of 12-(2-thiazolyl)-dodecene-1.

4. Oxidation of this dodecene with potassium permanganate, in acetone solution, gave the desired 11-(2-thiazolyl)-undecanoic acid, a thiazole analog of hydnocarpic acid, which it is hoped to have tested pharmacologically.

5. The reactions covered in items 1, 2 and 3 above, offer a means of preparing thiazoles carrying a long aliphatic chain in position 2.

NEW YORK, N. Y. RECEIVED FEBRUARY 19, 1943

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, UNIVERSITY OF CHICAGO]

Alkylation and Other Reactions of 9-Formylfluorene

BY WELDON G. BROWN AND BEN A. BLUESTEIN[1]

The aldehyde, 9-formylfluorene, obtained by condensing fluorene and ethyl formate,[2] behaves curiously on alkylation in that methyl sulfate reacts with the potassium salt to form the enol ether, whereas methyl iodide reacts to form 9-methylfluorene, the aldehyde group being eliminated as formate. Other alkyl halides, *viz.*, isopropyl bromide, cyclohexyl bromide and benzyl chloride, likewise yield the corresponding alkyl derivatives of fluorene with ease and in good yields.

Derivatives of enolic 9-formylfluorene are not new, the acetate, benzoate and similar compounds having been prepared by Wislicenus and coworkers,[2] but there are no previous examples in which the incoming group is attached to the carbon atom of the triad system. It can be assumed that the alkylation reactions with alkyl halides represent this second mode of reaction, complicated only by the condition that the tertiary aldehydes first formed must be sensitive to alkaline cleavage. In the synthesis of alkyl derivatives of fluorene from fluoreneoxalic ester by the method of Wislicenus,[2a] the intermediate

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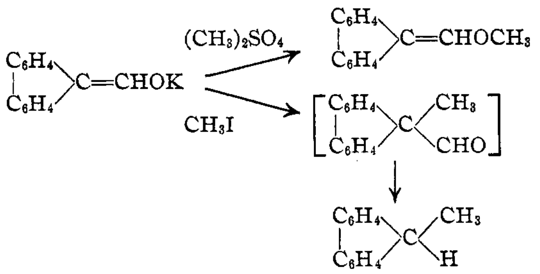
[1] This paper is taken from a dissertation submitted by Ben A. Bluestein to the Faculty of the Division of Physical Sciences of the University of Chicago in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry, December, 1941.

[2] (a) Wislicenus and Densch, *Ber.*, **35**, 759 (1902); Wislicenus and Waldmuller, *ibid.*, **42**, 785 (1909); (c) Wislicenus and Russ, *ibid.*, **43**, 2719 (1910); (d) Wislicenus and Weitmeyer, *Ann.*, **436**, 4 (1924).

alkylation product is isolated but we find that the experimental conditions can be adjusted so as to obtain the final product in one operation.



The reaction of 9-formylfluorene with formaldehyde, in alkaline solution, yields formate and 9-fluorenylcarbinol,[3] and while this has the outward characteristics of a crossed Cannizzaro reaction, these products doubtless result from a crossed aldol type condensation, followed by alkaline cleavage of the unstable tertiary aldehyde. Benzaldehyde and acetaldehyde do not react with 9-formylfluorene rapidly enough to compete with the decomposition reaction which the latter compound itself undergoes in alkaline solution.

The catalytic hydrogenation of 9-formylfluorene acetate, which had been investigated as a means of synthesizing 9-fluorenyl-carbinol, yields mainly 9-methylfluorene, together with a small amount of the expected 9-fluorenylcarbinol acetate. The latter is not further reduced under the conditions employed and is therefore not an intermediate in the formation of 9-methylfluorene. The benzoate of 9-formylfluorene behaves similarly on catalytic reduction, but with the benzylcarbonate derivative the only observed product is 9-methylfluorene. Evidently the ester linkage in these enol esters is highly susceptible to hydrogenolysis.

Experimental

9-Formylfluorene.—Following the directions of Wislicenus and Waldmuller,[2b] fluorene and ethyl formate were condensed in ether solution, with potassium ethoxide as the condensing agent. Notwithstanding the statement of Wislicenus and Densch[2a] to the contrary, sodium ethoxide was also found to be effective as a condensing agent, but the yields were somewhat poorer, namely, 65%, as compared with 80–90% when potassium ethoxide was used. Because of the poor keeping qualities of the aldehyde, it was prepared in small batches as needed; viscous yellow liquid, b. p. 189–192° (10 mm.) [lit.[2b] b. p. 196–197° (14 mm.)].

Methyl Ether of 9-Formylfluorene.—To 10.0 g. (0.051 mole) of 9-formylfluorene was added a solution of 6.5 g. (0.12 mole) of potassium hydroxide in 50 cc. of water, and the mixture was filtered to remove traces of insoluble material. To the red-brown aqueous solution was added 7.0 g. of dimethyl sulfate. Within a few minutes the mixture became opaque, an oil separated and solidified, and the supernatant liquid became yellow. The solid product, after washing with water and twice recrystallizing from 95% alcohol, was obtained as light yellow needles melting at 104°. The yield was 6.5 g., or 62% of theoretical. The substance reacted instantly with a solution of bromine in carbon tetrachloride, and with potassium permanganate in acetone solution, and did not react with Tollens' reagent. These observations, together with the analytical data, established the identity of the compound as the methyl ether of 9-formylfluorene.

Anal. Calcd. for $C_{15}H_{12}O$: C, 86.53; H, 5.81. Found: C, 86.53; H, 5.95.

The compound is light-sensitive, and, if unprotected, turns dark in color and liquefies within a few days.

9-Methylfluorene.—To 10.0 g. (0.051 mole) of 9-formylfluorene was added a solution of 6.5 g. (0.116 mole) of potassium hydroxide in 50 cc. of water, and to the resulting solution was added 7.5 g. (0.055 mole) of methyl iodide. After shaking for about one minute an emulsion was formed and upon standing a liquid separated which solidified on cooling in an ice-bath. There was obtained, after recrystallization from methanol, 6.9 g. (75%) of almost white needles, m. p. 41–44°. A second recrystallization yielded white needles, m. p. 44.5° (lit.[4] m. p. 45°).

9-Isopropylfluorene.—The reaction was carried out in a manner similar to the preceding one, using an equivalent amount of isopropyl bromide in place of methyl iodide, except that 50 cc. of alcohol was added in order to form a homogeneous solution. The reaction mixture was allowed to stand for several hours, during which time a small quantity of oil separated, and was then refluxed for thirty minutes. The addition of 100 cc. of water caused the separation of a larger quantity of the oil which solidified upon cooling. Recrystallization of the product from methanol yielded 6.3 g. (60%) of light yellow needles, m. p. 52–54°, and a second recrystallization resulted in a colorless product, m. p. 54–55° (lit.[5] m. p. 53–55°).

9-Cyclohexylfluorene.—The preparation of this compound, from cyclohexyl bromide and 9-formylfluorene, was carried out in essentially the same manner as the preceding one save that the solution was refluxed for three hours. The product, after recrystallization from 95% ethanol, was obtained as white needles, m. p. 113–115°, in 55% yield. A second recrystallization raised the m. p. to 115–116°.[6]

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[3] Previously synthesized by a Meerwein–Ponndorff reduction of the aldehyde (Brown and Bluestein, THIS JOURNAL, **62**, 3256 (1940)).

(4) Wislicenus and Mocker, *Ber.*, **46**, 2780 (1913).

(5) Maitland and Tucker, *J. Chem. Soc.*, 2559 (1929).

(6) Miller and Bachman, THIS JOURNAL, **57**, 766 (1935), reported the preparation of 9-cyclohexylfluorene from 9-chlorofluorene and cyclohexylmagnesium bromide but a discrepancy was found to exist between the properties of their compound, m. p. 102–103°, and the compound described above. A mixed melting point, with a sample kindly furnished by Dr. Bachman, left no doubt that the two compounds are not identical, and since the analytical data for the product obtained by these authors are not consistent with the assigned formula, it is concluded that an error has been made in the identification.

Anal. Calcd. for $C_{19}H_{20}$: C, 91.88; H, 8.12. Found: C, 91.62; H, 8.17.

9-Benzylfluorene (from 9-formylfluorene).—To the red solution obtained by dissolving 6.5 g. (0.12 mole) of potassium hydroxide and 10.0 g. (0.051 mole) of 9-formylfluorene in 50 cc. of water was added a solution of 7.0 g. (0.055 mole) of benzyl chloride in 50 cc. of 95% alcohol. After standing for ninety minutes, during which time a light yellow solid had precipitated, the mixture was filtered, and the product, after washing and drying, was recrystallized from a benzene–ligroin mixture. There resulted 10.0 g. of hard white crystals, m. p. 131–133°, a 77% yield of 9-benzylfluorene. A second recrystallization from ligroin raised the m. p. to 132–133° (lit.[7] m. p. 130–131°).

9-Benzylfluorene (from 9-Fluoreneoxalic Ester).—To a solution of 2.4 g. of 9-fluoreneoxalic ester in 8 cc. of aqueous 10% sodium hydroxide, was added 1.4 g. of benzyl chloride and enough alcohol to form a single phase. After refluxing the solution for thirty minutes, the product was isolated as before, yielding 2.0 g. (80%) of 9-benzylfluorene, m. p. 133°.

9-Fluorenylcarbinol (Formaldehyde Method).—Five grams of 9-formylfluorene was dissolved in 20 cc. of 10% sodium hydroxide solution, and to the resulting solution 10 cc. of 10% aqueous formaldehyde was added slowly with vigorous stirring. An oil separated which soon solidified. The product, after recrystallization from high boiling ligroin, was obtained as colorless needles, m. p. 100–101°; yield, 67%. It was identical with samples of 9-fluorenylcarbinol previously prepared by reduction of 9-formylfluorene with aluminum isopropoxide.

Hydrogenation of 9-Formylfluorene Acetate.—Five grams of 9-formylfluorene acetate was suspended in 100 cc. of alcohol, 0.1 g. of platinum oxide was added, and the mixture was shaken with hydrogen at 3 atmospheres pressure for two hours. The organic material in suspension dissolved as the hydrogenation proceeded. Evaporation of the filtrate yielded a residual oil having the odor of acetic acid. The oil was taken up in benzene, washed with dilute sodium hydroxide solution, and, after evaporation of the benzene, was subjected to vacuum distillation. The distillate solidified, melting at 43–44° after recrystallization from methanol, and was identified as 9-methylfluorene. The residue from the vacuum distillation, after recrystallizing twice from ligroin, had a m. p. at 84–85°. A mixed melting point with 9-fluorenylcarbinol acetate, prepared from 9-fluorenylcarbinol, acetic anhydride, and sodium acetate, showed no depression.

The saturated ester, 9-fluorenylcarbinol acetate, when suspended in alcohol with platinum oxide and shaken with hydrogen at 3 atmospheres pressure, was recovered unchanged.

The benzoate of 9-formylfluorene, when subjected to catalytic hydrogenation under similar conditions for a period of three hours, yielded, in addition to unchanged starting material, benzoic acid, 9-methylfluorene, and a white solid, m. p. 93.5°, identified by mixed melting point with an authentic specimen as the benzoate of 9-fluorenylcarbinol.

Benzyl Diphenylene-ethylene Carbonate.—To an aqueous solution of the potassium salt of 9-formylfluorene, prepared from 13.6 g. of fluorene, was added 14 cc. of benzyl chloroformate. After a few seconds a white solid precipitated, which, after recrystallization from benzene, melted at 149.5°.

Anal. Calcd. for $C_{22}H_{16}O_3$: C, 80.48; H, 4.91. Found: C, 80.61; H, 5.07.

Catalytic hydrogenation of this ester proceeded very slowly, possibly because of its extreme insolubility in alcohol. The only product isolated was 9-methylfluorene in small amount.

Summary

The potassium salt of 9-formylfluorene reacts with methyl sulfate to form an enol ether, but with alkyl halides the alkyl group enters position 9 in the fluorene nucleus with concurrent elimination of the formyl group. The reaction with formaldehyde, which yields 9-fluorenylcarbinol, is interpreted in a similar way. This method for the preparation of 9-fluorenylcarbinol is superior to others which are discussed.

CHICAGO, ILLINOIS RECEIVED MARCH 10, 1943

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[7] Thiele and Henle, *Ann.*, **347**, 298 (1906).