[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Higher Benzenoid Hydrocarbons. III. The Isomeric Monobromo-9-fluorenols and Monobromofluorenes

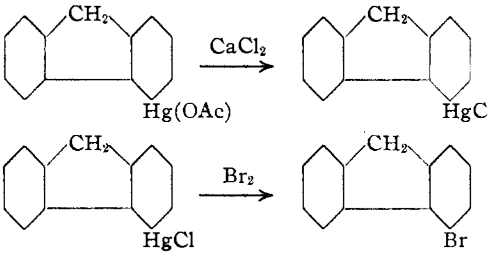
BY HARRY F. MILLER AND G. BRYANT BACHMAN

The reduction of the bromofluorenones with zinc dust and alcoholic ammonia leads to the formation of the corresponding bromo-9-fluorenols in excellent yields. However, the subsequent reduction of these bromofluorenols to bromofluorenes is not always readily accomplished because of the lability of the bromine atoms particularly in the 3-position. We found that with hydriodic acid and phosphorus 3-bromo-9-fluorenol yields fluorene only. Montagne and Moll[1] have also called attention to the ease with which the bromine in this position is removed on reduction with sodium amalgam in boiling alcohol. This lability is rather remarkable in view of the equally great stability of the bromine atom in the 2-position. It was shown previously[2] that 2-bromofluorene either does not yield a Grignard reagent or does so with unusual difficulty. Loevenich, Becker and Schröder[3] have shown that toward potassium phenolate and sodium acetate 2-bromofluorene is only about 50–75% as reactive as bromobenzene and is similar to meso-bromoanthracene in stability. The contrast between 2- and 3-bromofluorenes is reminiscent of the similar contrast in stability offered by 1- and 2-bromonaphthalenes.

Preparation of the bromofluorenes by direct reduction of the bromofluorenones by Clemmensen's method is highly satisfactory even in the case of 3-bromofluorene. Of the five possible monobromofluorenes only two, 2-bromofluorene[4] and 9-bromofluorene[5] have been prepared previously. In the present work 3- and 4-bromofluorenes have been obtained for the first time by reduction methods from the bromofluorenones described in the preceding paper.

Mercuration of Fluorene

Having once established the structure of the isomeric bromofluorenes by nuclear synthesis, it was decided to determine the position or positions in which fluorene mercurates, by heating the hydrocarbon with mercuric acetate and converting the product into one or more bromofluorenes as the case might be. As is well known, the entering mercuric group often attaches itself to a different position than that attacked by other reagents such as the halogens, nitric acid, sulfuric acid, etc. In the case of fluorene all of these latter reagents enter the 2-position first and the 7-position next, so that with bromine for example, the 2- and the 2,7-derivatives only are obtained by direct substitution. Goswami and Das-Gupta[6] report that fluorene reacts with mercuric acetate, but the structure of the product was not elucidated. We find that in the presence of acetic acid fluorene mercurates predominantly in the 4-position. In the absence of solvents some of the 3-isomer is also formed. By treatment of the product with alcoholic calcium chloride and subsequent bromination of the fluorene mercurichloride, good yields of 4-bromofluorene were obtained.



3-Bromofluorene was also prepared by this method.

An interesting point may be raised in view of the above results. Conant and Wheland[7] and others have offered the idea that in the reaction

$$\mathrm{RH} + \mathrm{R'Na} \longrightarrow \mathrm{RNa} + \mathrm{R'H}$$

the hydrocarbon RH may be regarded as a very weak acid, which is, however, relatively stronger than R'H for it is able to abstract Na from the salt R'Na. For instance, fluorene is a stronger acid than triphenylmethane, for it abstracts sodium from triphenylmethyl–sodium to form fluoryl-9-sodium. A whole series of compounds in the order of their acidities may be formed by

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(1) Montagne and Moll, *Rec. trav. chim.*, **32**, 164 (1913).

(2) Miller and Bachman, THIS JOURNAL, **57**, 766 (1935).

(3) Loevenich, Becker and Schröder, *J. prakt. Chem.*, **127**, 248 (1930).

(4) Courtot and Vignati, *Bull. soc. chim.*, [4] **41**, 58 (1927).

(5) Wanscherdt, *Ber.*, **59**, 2092 (1926).

(6) Goswami and Das-Gupta, *J. Ind. Chem. Soc.*, **8**, 475 (1931).

(7) Conant and Wheland, THIS JOURNAL, **54**, 1212 (1932).

such competitive reactions. Gilman[8] suggests further that if metalation is a function of relative acidities, then the most acid hydrogen atom in an aromatic compound is that replaced in the metalation reaction. Accordingly, he calls the hydrogen atom in the 4-position in dibenzofuran more acidic than those in the 2- or 3-positions. Such a statement is inapplicable to fluorene, for, if it were true, fluorene should mercurate in the 9-position. It is recognized that the hydrogen atoms in the methylene bridge are very active, as shown by many condensation reactions, by the fact that ethane is liberated from ethylmagnesium bromide to form fluoryl-9-magnesium bromide and by the fact that fluorene will form fluoryl-9-sodium by reaction with sodium triphenylmethyl. Gilman's hypothesis might be modified to state that mercuration may only determine the most acidic hydrogen atom on a truly aromatic hydrocarbon ring.

The Dibromo and Chlorobromofluorenes

By saturating alcoholic solutions of the bromo-9-fluorenols with hydrogen bromide or hydrogen chloride the corresponding x-9-dibromo- and x-bromo-9-chlorofluorenes were obtained. The properties of these and the other fluorene derivatives prepared are indicated in Table I. Further work on the preparation and reactions of the Grignard reagents of the isomeric bromofluorenes is now under way.

TABLE I

BROMO DERIVATIVES OF FLUORENE

Substance	Cryst. form	Yield, %	M.p., °C.	Anal. for halogen Calcd.	Anal. for halogen Found
2-Bromofluorenol[a]	Fluffy needles	97	130		
3-Bromofluorenol	White plates	85	142–145	30.62	30.45
4-Bromofluorenol	Feathery needles	92	149–150	30.62	30.57
2-Bromofluorene[a]	White plates	82	110		
3-Bromofluorene	Short needles	Quant.	90–91	32.61	32.51
4-Bromofluorene	Needles	80	165	32.61	32.49
2,9-Dibromofluorene	Fluffy needles	Quant.	107.5–108.5	49.34	49.32
3,9-Dibromofluorene	Matted needles	92	124–125	49.34	49.17
4,9-Dibromofluorene	Thick needles	83	194–195	49.34	49.22
2-Bromo-9-chlorofluorene[a]	Long needles	Quant.	102		
3-Bromo-9-chlorofluorene	Fluffy needles	87	116–117	41.28	41.08
4-Bromo-9-chlorofluorene	Matted needles	86	141–142	41.28	41.11

[a] Previously recorded in the literature.

Experimental

Reduction of Bromofluorenones to Bromofluorenols with Zinc and Alcoholic Ammonia.—The reduction of one isomer only will be described since the procedure in all other cases was similar.

Three and five-tenths grams of 4-bromofluorenone, 14 g. of zinc dust, 110 cc. of ethanol and 20 cc. of concentrated ammonium hydroxide were refluxed for one hour and filtered hot. Water was added to precipitate a gelatinous mass of 4-bromofluorenol. This was filtered by suction, pressed down well, and washed with 40% ethanol. After drying and recrystallizing from benzene, 3.2 g. of feathery white needles, m. p. 149–150°, was obtained, a 91.5% yield.

Reduction of Bromofluorenols to Bromofluorenes.—Although 2-bromofluorene is known, its preparation from the corresponding fluorenol has never been recorded.

One gram of 2-bromofluorenol, 1 g. of red phosphorus and 1 g. of iodine were refluxed for two hours in a solution of 20 cc. of glacial acetic acid and 2 cc. of water. The hot solution was filtered and added to 200 cc. of cold water containing 4 cc. of saturated sodium bisulfite solution. The white precipitate which formed was filtered after standing for one hour. Recrystallization from alcohol yielded a pure product melting at 110° alone or when mixed with an authentic sample of 2-bromofluorene. The material weighed 0.75 g., corresponding to an 82% yield.

Reduction of Bromofluorenones to Bromofluorenes.—One gram of 3-bromofluorenone and 20 cc. of ethanol were added portionwise over a three-hour period to a refluxing mixture of 7 cc. of concentrated hydrochloric acid, 3 cc. of water and 25 g. of amalgamated zinc. During this period 10 cc. of concentrated hydrochloric acid also was added portionwise. The mixture was refluxed three more hours, and the liquid portion decanted hot. The zinc was washed with two 5-cc. portions of hot ethanol, and the washings added to the main solution. On cooling short white needles formed, which were recrystallized from hot ethanol. Long white needles formed, melting at 90–91°. The yield was practically quantitative.

Preparation of x-9-Dibromofluorenes.—A solution of 3 g. of 3-bromofluorenol in 15 cc. of ethanol was saturated in the cold with dry hydrogen bromide. The mixture was stoppered tightly and left in the ice-bath, which was allowed to warm up overnight. Short stubby needles of 3,9-dibromofluorene formed which, after two days of standing, were filtered at the pump, washed with 50% alcohol, and dried. They melted at 124–125°. A second small crop was obtained by diluting the filtrate with water. The total yield was 3.1 g. (92%).

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(8) Gilman and Young, THIS JOURNAL, **56**, 1415 (1934).

Preparation of *x*-Bromo-9-chlorofluorenes.—Two grams of 4-bromofluorenol was dissolved in 10 cc. of ethanol and saturated in the cold with dry hydrogen chloride. The container was well stoppered and left in the ice-bath, which was allowed to come to room temperature. Unlike the other chlorides, this one precipitated first as an oil, and it was necessary to add a few drops of water to the mixture and place it in an ice-chest to induce it to crystallize. The white matty needles were filtered by suction, washed with 50% ethanol and recrystallized from benzene to give 1.94 g. of white needles melting at 141–142°, an 86% yield.

Mercuration of Fluorene in the Absence of a Solvent.—Eighty-three grams of fluorene was melted in a 2-liter round-bottomed flask and 159 g. of mercuric acetate added as soon as the temperature of the melt reached 125°. By means of an oil-bath the temperature of the melt was raised to 145°, at which point acetic acid began to distil (hood). The melt was held at this temperature for twenty-five minutes, at the end of which time the reaction had ceased, as indicated by the cessation of acetic acid fumes. The mixture was cooled to 110° and 500 cc. of glacial acetic acid added. The fluorene mercuriacetate went into solution easily. The solution was immediately treated with 2500 cc. of a saturated alcoholic calcium chloride solution. The mixed fluorene monomercurichlorides immediately precipitated in a voluminous mass, which was filtered hot and washed with glacial acetic acid, hot benzene, more glacial acetic acid, and finally with water. The air-dried white powder weighed 136 g., a 66% yield. However, 16 g. of pure fluorene was recovered from the filtrate, which raised the yield by difference to 81.4%. The product did not melt below 225°, and was shown to be a mixture of the 3- and 4-isomers in the ratio of approximately 3:1 by conversion of the mixture into the corresponding bromofluorenes and separating by recrystallization. The separation of the mixed mercurichlorides was not attempted due to their insolubility in all solvents tried.

The product obtained did not correspond with that of Goswami and Das-Gupta. These authors describe their unknown fluorene mercurichloride as a light pink solid melting at 130–132° with decomposition.

Bromination of the Mercurated Fluorene Mixture.—Eighty grams of the mixed mercurichlorides, obtained by mercuration of fluorene in the absence of a solvent, was suspended in 150 cc. of glacial acetic acid in a 500-cc. round-bottomed flask. Thirty-two grams of bromine in 25 cc. of glacial acetic acid was added with efficient stirring over a seven-hour period. The mixture was heated to boiling and filtered hot. Hydrogen sulfide was passed into the hot filtrate to remove dissolved mercury compounds, and the mixture was filtered again. As the filtrate cooled, a white crystalline precipitate slowly formed. This was removed by filtration and several more crops obtained by successive evaporation of the solvent. Each crop melted over a wide temperature range. The combined product totalling 35.4 g. (72.2% yield) was added to a mixture of 500 cc. of ligroin and 25 cc. of benzene. This mixture was boiled for five minutes and filtered hot, approximately two-thirds of the solid dissolving. On evaporation of the solvent a white waxy solid was obtained which was recrystallized from 75 cc. of glacial acetic acid. The 22.1 g. (45% yield) of white flaky material so obtained melted at 148–149°, and proved to be 4-bromofluorene. The ligroin insoluble portion was recrystallized twice from glacial acetic acid to give 7.2 g. (14% yield) of 3-bromofluorene, m. p. 88–94°.

Mercuration of Fluorene in Acetic Acid.—Eighty-three grams of fluorene, 159 g. of mercuric acetate and 250 cc. of glacial acetic acid were refluxed for twelve hours. A pink-colored solid settled out during the last six hours. The solution was filtered hot and 250 cc. of a saturated alcoholic calcium chloride solution added with stirring. A pink-colored precipitate formed immediately. This was filtered and washed with glacial acetic acid, hot benzene, glacial acetic acid and finally water. The color was not removed by this treatment. The solid after being air-dried weighed 40 g. (63% yield based on the fluorene used). The product melted at 235–240° with darkening at 165°. It was shown by bromination to be practically pure fluorene-4-mercurichloride.

Bromination of Fluorene-4-mercurichloride.—Forty grams of fluorene-4-mercurichloride suspended in 200 cc. of glacial acetic acid was brominated with 14.5 g. of bromine in 25 cc. of glacial acetic acid during an eight-hour period. The product was isolated as before. All of it melted from 145–148° and recrystallization from acetic acid gave white needles; m. p. 165°; yield 16.1 g. (66%). 4-Bromofluorene also crystallizes occasionally in white plates.

Oxidation of 3- and 4-Bromofluorenes.—In order to establish further the structure of the 3- and 4-bromofluorenes obtained through mercuration, they were converted into the corresponding bromofluorenones by oxidation with sodium dichromate and acetic acid. The products so obtained were identical with the bromofluorenones obtained in the preceding paper by ring closure methods.

Five and six-tenths grams of 4-bromofluorene and 16 cc. of glacial acetic acid were placed in a 120-cc. round-bottomed flask fitted for reflux. The mixture was brought to a vigorous boil and a hot mixture of 20 g. of technical sodium dichromate, 10 cc. of water and 28 cc. of glacial acetic acid was added by means of a dropping funnel over a one-half hour period, in such a manner that no lumps of unreacted material separated. After refluxing vigorously for three hours, the hot material was poured into 200 cc. of ice and water, allowed to stand for two hours, filtered by suction and washed, first with 4% sulfuric acid, and then several times with water. The air-dried material was dissolved in 15 cc. of benzene and left to crystallize. Five and nine-tenths grams (96%) of yellow needles of the ketone was obtained, melting at 185–187°.

Summary

1. The 2-, 3- and 4-monobromo-9-fluorenols and monobromofluorenes have been prepared by the reduction of the corresponding monobromofluorenones.

2. The monobromo-9-fluorenols have been converted into the corresponding *x*,9-dibromofluorenes and *x*-bromo-9-chlorofluorenes.

3. The mercuration of fluorene with mercuric acetate in the presence and in the absence of

a solvent has been studied. The preparation of 3- and 4-bromofluorenes from the resulting fluorene mercury derivatives has been described.

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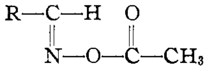
The Removal of Hydrogen and Acid Radicals from Organic Compounds by Means of Bases. II. The Removal of Acetic Acid from Acetyl-aldoximes by Alkalies

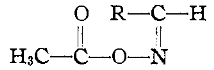
BY CHARLES R. HAUSER AND EARL JORDAN

As part of a general program on the removal of the elements of acids from organic compounds by means of bases it was of interest to study the removal of acetic acid from geometrically isomeric acetyl-aldoximes, (I) and (II).



$R-CH=N-O-C(=O)-CH_3$

(I) *syn* (α)



$H_3C-C(=O)-O-N=CH-R$

(II) *anti* (β)

It is well known that in the presence of alkali one of these isomers eliminates acetic acid more readily than the other. Indeed, this reaction is used to distinguish a pair of geometrically isomeric aldoximes; the isomer whose acetyl derivative more readily forms nitrile is designated the β-, whereas the other is designated the α-isomer. Formerly, it was assumed that the unstable (β-) acetate had the *syn* configuration simply because the hydrogen atom and acetate group are in closer proximity in (I) than in (II); this view was based presumably on the assumption that the elements of acetic acid were removed simultaneously. At the present time, however, the unstable (β-) acetate is assigned the *anti* configuration (II), whereas the more stable (α-) isomer is assigned the *syn* (I). This view is based on a good deal of experimental evidence[1] accumulated during the past ten years. It is supported also on theoretical grounds on the basis of the hypothesis that, in the formation of nitrile, a proton is removed first by the action of alkali followed by the release of the acetate ion. According to Mills,[2] after the removal of a proton, the movement of the nitrogen nucleus to form the triple bond of the nitrile favors the release of the acetate ion, only in the case of the isomer with configuration (II). It should be pointed out also that the proximity of the acetate group to the hydrogen atom in (I) might offer some steric hindrance to the removal of the proton, thereby hindering the release of the acetate ion and formation of nitrile.

Although the reactions of acetyl aldoximes with alkalies have been studied extensively in connection with the determination of configurations of aldoximes there appears to have been relatively little quantitative work carried out under controlled conditions. In this investigation we have studied these reactions at definite temperatures and in most cases have isolated almost quantitative yields of products. The results are given in the following tables. The melting points of the crude products and those recorded in the literature are listed consecutively following the yields. In most cases the melting points of the crude products were either practically the same as those reported in the literature or were raised to these values after one recrystallization.

Discussion

It is often stated or implied in the literature that acetyl-α-, and acetyl-β-aldoximes react entirely differently toward alkali, that the α- give only oxime, and the β- only nitrile. Recently, however, it has been shown[3] that with sodium hydroxide certain acetyl-β-aldoximes give both nitrile and oxime, the yields of these products being dependent on the temperature, and now it has been found that at the temperature of the boiling water-bath at least certain acetyl-α-aldoximes with alkali give some nitrile in addition to the corresponding oxime.

It can be seen from Table I that, in general, acetyl-β-benzaldoximes with 2 N sodium hydroxide gave higher yields of oxime than nitrile at 0°, but greater yields of nitrile at 30°. These results confirm and extend those previously reported.[3]

In Table II are given the yields of products obtained from the reactions of certain acetyl-α-benzaldoximes with 2 N sodium hydroxide. It can be seen that at 61–64° the 2-nitro derivative

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[1] For review of evidence, see Freudenberg, *Stereochemie*, **7**, 974–979 (1933); Perkin and Kipping, "Organic Chemistry," Part III, 1934, pp. 661–663.

[2] Mills, *J. Soc. Chem. Ind.*, **51**, 755 (1932).

[3] Hauser and Sullivan, THIS JOURNAL, **55**, 4611 (1933).