

with the rate of heating. With very slow heating, they melt a few degrees lower (1–4°).

Cleavage of Phenyl-naphthylborinic Acid with Dimethylaminoethanol.—A 0.500-g. sample of aminoethyl phenyl-naphthylborinate (prepared from butyl naphthaleneboronic acid as described in procedure b) was shaken with ether and 6 *N* hydrochloric acid until all of the solid had dissolved. The ether layer was then evaporated on a steam-bath and a solution of 2 ml. of β -dimethylaminoethanol in 2 ml. of 95% ethanol was added to the residue. After this solution had been warmed on a steam-bath for ten minutes, 25 ml. of water was added over a period of five minutes while the flask was still on the steam-bath. A milky, white solid separated and on cooling it coagulated to an easily filtered precipitate, which after drying weighed 0.200 g. (86%) and was shown to be naphthalene by its melting point (79–80°) and a mixed melting point determination with commercial naphthalene. The filtrate from the naphthalene was clear. Acidification and ether extraction yielded 0.181 g. (82%) of benzenboronic acid, m.p. 209–215°. The melting point was not depressed when the sample was mixed with pure benzenboronic acid, but it was depressed over 40° when the sample was mixed with naphthaleneboronic acid.

This cleavage reaction proceeded even at room temperature. Thus a 0.500-g. sample of the aminoethyl borinate treated as described above except that the mixture was maintained at room temperature gave a 19% yield of naphthalene. In this case dilute sodium hydroxide was added to the reaction mixture after the addition of water in order to dissolve unreacted borinic acid. From a similar reaction at room temperature for which the water and sodium hydroxide were added within a few seconds after the dimethylaminoethanol had been added, no naphthalene was obtained. Only a slight turbidity remained after addition of the sodium hydroxide. It is apparent therefore that the naphthalene formed during the treatment with dimethylaminoethanol and not before the addition of this reagent.

A 0.500-g. sample of aminoethyl phenyl-naphthylborinate was heated for 10 minutes on a steam-bath with 2 ml. of ethanolamine and 2 ml. of alcohol. The ester did not dissolve in this solution. After cooling, it was filtered off and dried; weight of recovered ester, 0.471 g. (94%). Therefore the ethanolamine did not cleave the carbon boron bond in this compound as did dimethylaminoethanol. The insolubility of the aminoethyl ester in the reaction mixture may be responsible for the lack of reaction.

Cleavage of Phenyl-naphthylborinic Acid by Bromine.—A modification of the bromine degradation described by Kuivila and Soboczenski⁶ was employed. Phenyl- α -naph-

(6) H. G. Kuivila and E. J. Soboczenski, *THIS JOURNAL*, **76**, 2575 (1954).

thylborinic acid, obtained as an oil by the acid hydrolysis of 4.99 g. (0.018 mole) of the ethanolamine ester (prepared from butyl benzenboronate, procedure a), was mixed with 25 ml. of 3.3 *M* acetic acid containing 3.2 g. (0.08 mole) of sodium fluoride and 4.92 g. (0.06 mole) of sodium acetate. A solution of 16.0 g. (0.1 mole) of bromine and 14.4 g. of potassium bromide in 50 ml. of 3.3 *M* acetic acid was added over a two-hour period to the stirred, refluxing solution. The resulting mixture was refluxed for an additional 30 minutes, cooled and treated with sodium sulfite to remove unreacted bromine. It was then made alkaline and steam distilled for 30 minutes. The steam-volatile distillate was taken up in 20 ml. of petroleum pentane and 3 ml. of ether, dried over potassium carbonate, and distilled. A 68% yield (1.92 g.) of bromobenzene, b.p. 149–164°, n_{27}^{20} 1.5528, was obtained. The higher boiling residue amounted to 1.08 g. This residue was combined with the organic material obtained by steam distilling the original reaction mixture for an additional 30 minutes, and redistilled. There was obtained 1.8 g. of α -bromonaphthalene, b.p. 153–156° at 27 mm., n_{30}^{20} 1.6442. The identity of the bromobenzene and bromonaphthalene was established by a comparison of their spectra with the infrared spectra of authentic samples of these compounds. From the residue there was isolated 0.17 g. of a solid (m.p. 67–70°) which after recrystallization melted at 74–76°. This melting point was not depressed when the sample was mixed with pure 1,4-dibromonaphthalene (m.p. 82–85°) prepared by the bromination of α -bromonaphthalene.

Cleavage of II with Other Reagents.—To 0.5 g. of the borinate (prepared by procedure a) suspended in 10 ml. of 50% alcohol was added 5 ml. of 30% hydrogen peroxide. After a few minutes the mixture began to warm up spontaneously, and the solid ester became a liquid. On cooling, the oil resolidified, was filtered (weight 0.1 g., m.p. 88–90°), and recrystallized from ethanol-water. The melting point of the compound thus obtained (m.p. 92°) was not depressed when the sample was mixed with α -naphthol.

From the distillate of a steam distillation of a solution of 1 g. of the borinate and 2 g. of zinc chloride in 20 ml. of water was isolated naphthalene, which after recrystallization weighed 0.28 g. (49% yield). The first crop of the crystals from the recrystallization melted at 80–81°, and the third crop, at 79–80°. Mixed melting points with naphthalene showed no depression. In the absence of the zinc chloride the cleavage was very slow. Thus the steam distillation of the ester in dilute hydrochloric acid yielded only a trace of naphthalene and the aminoethyl borinate was recovered in 75% yield after the solution had been made basic.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

Organoboron Compounds. IV.¹ Aminoethyl Diarylborinates

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A practical procedure has been developed for the preparation of aminoethyl diphenylborinate. This involves the reaction of phenylmagnesium bromide with butyl borate at low temperature, isolation of butyl diphenylborinate as a complex with ammonia, and conversion of the ammonia complex to the aminoethyl ester with ethanolamine. Aminoethyl bis-(*p*-bromophenyl)-borinate was prepared by similar techniques. Solid derivatives of arylboronic acids may be obtained by esterifying them with diethanolamine.

The diarylborinic acids represent an important class of organoboron compounds since projected syntheses for a variety of complex types of arylboron compounds involve them as intermediates. Yet no satisfactory procedure for preparing and characterizing these substances has been described. Several diarylborinic acids have been re-

ported²; however, the isolation procedures were generally poor, the yields were low or unspecified, and in some cases there were marked divergences in the properties reported for a particular compound. The status of the parent member of the

(1) This material was presented at the meeting of the American Chemical Society in New York, September, 1954. For paper III in the series see *THIS JOURNAL*, **76**, 4047 (1954), and paper II, *ibid.*, **76**, 4147 (1954).

(2) (a) A. Michaelis, *Ber.*, **27**, 244 (1894); (b) A. Michaelis and E. Richter, *Ann. Chem.*, **315**, 26 (1901); (c) W. König and W. Scharnbeck, *J. prakt. Chem.*, **128**, 153 (1930); (d) N. N. Melnikov and M. S. Robil'sbaya, *J. Gen. Chem., USSR*, **8**, 1768 (1938); *C. A.*, **33**, 4970 (1930); (e) N. N. Melnikov, *J. Gen. Chem., U.S.S.R.*, **6**, 636 (1936); *C. A.*, **30**, 5571 (1936).

TABLE I
 DIETHANOLAMINE ESTERS OF ARYLBORONIC ACIDS

Boronic acid	Derivatives		Boron, %		Nitrogen, %		Neut. equiv.	
	Yield, %	M.p., °C.	Calcd.	Found ^a	Calcd.	Found	Calcd.	Found
C ₆ H ₅ B(OH) ₂	85	214–215	3.66	5.70	7.33	7.54	191	192
BrC ₆ H ₄ B(OH) ₂	58	255–256	4.01	4.08	5.19	5.66	270	271
CH ₃ OC ₆ H ₄ B(OH) ₂	55	216–218	4.89	4.94	6.34	6.49	221	208
α-C ₁₀ H ₇ B(OH) ₂	88	242–243					241	245

series, diphenylborinic acid, has been especially questionable. Michaelis claimed, in 1894, to have isolated this substance as a solid melting at 264–267° by hydrolysis of diphenylboron chloride.^{2a} A few years later Michaelis and Richter^{2b} obtained an oil, also believed to be diphenylborinic acid, by hydrolysis of diphenylboron bromide. Finally, in 1930, König and Scharrnbeck^{2c} reported that they had obtained diphenylborinic acid as a low melting solid (m.p. 57.5°). They used the reaction of phenylmagnesium bromide with isobutyl borate and separated the products, after hydrolysis, by distillation. Diphenylborinic acid was reported to distil at 150° at 20 mm.

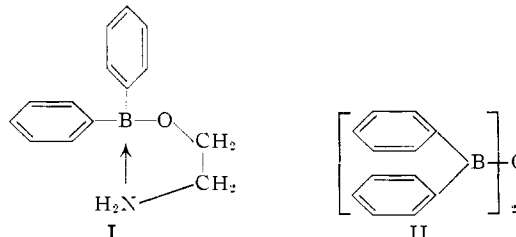
We first attempted, but without success, to prepare and isolate diphenylborinic acid by the procedure described by König and Scharrnbeck.^{2c} The only solid organoboron compounds obtained from this reaction and from several related Grignard reactions were benzeneboronic acid and triphenylborine. We then observed that a crystalline substance (dec. 64–67°) could be precipitated by passing ammonia into an ether solution of the products of the Grignard reaction (subsequent to hydrolysis and distillation). This compound proved to be the ammonia complex of butyl diphenylborinate (Ph₂BOC₄H₉:NH₃). It was obtained in 23% yield from a Grignard reaction carried out at 35°, and in 49% yield from a reaction conducted at –60°. Ammonia complexes of borines are well known, but to our knowledge, this is the first example of such a compound formed by a borinate.

While this ammonia complex was useful in separating the borinate, it was not a satisfactory derivative for characterization purposes since it did not melt sharply and gradually decomposed, even at room temperature. It could be converted in 80–90% yield, however, to β-aminoethyl diphenylborinate by the action of ethanolamine in toluene or an ethanol–water solution. Here the nitrogen is held by covalent bonds in a position favorable for coordination with the boron atom. It is noteworthy that this ester could be prepared in the presence of water and even recrystallized from water without hydrolysis. The aminoethyl ester was an excellent derivative; it was prepared easily, could be recrystallized readily, melted sharply, analyzed well, and over a period of several months it showed no sign of decomposition.

The physical properties and stability to air oxidation indicate that the nitrogen is coordinated to the boron atom in this compound. As a molecular weight determination in camphor showed the borinate to be monomeric, the structure seems best formulated as I.

β-Aminoethyl diphenylborinate was hydrolyzed with dilute hydrochloric acid to the borinic acid,

which separated as an oil that did not crystallize. This oil distilled as diphenylborinic anhydride (II), b.p. 210–213°, when heated at 1 mm. pressure. It therefore appears that neither Michaelis' compound which melted at 264° nor König's compound which boiled at 150° at 20 mm. could have been diphenylborinic acid.



Aminoethyl bis-(*p*-bromophenyl)-borinate was obtained in 17% yield from a reaction of *p*-bromophenylmagnesium bromide with butyl ethyleneborate. No doubt, with further investigation of the reaction conditions this yield could be improved.

Since solid esters were obtained by esterifying the arylborinates with ethanolamine and by esterifying boric acid with triethanolamine,³ the reaction of diethanolamine with some arylboronic acids was investigated. Sharp melting compounds which should be useful as derivatives of the boronic acids were obtained. The data are summarized in Table I.

Experimental

Preparation of Isobutyl Diphenylborinate and Precipitation by Ammonia.—The reaction conditions of König and Scharrnbeck were used with the modification that the Grignard reagent was added to the isobutyl borate. Previously, the borate had been added to the Grignard reagent.^{2c}

A solution of phenylmagnesium bromide (1.2 *M*, 475 ml.) was added slowly with stirring to 60.2 g. (0.284 mole) of isobutyl borate in 150 ml. of ether at room temperature. In this and all subsequent Grignard reactions a nitrogen atmosphere was used. The ether solvent refluxed slowly during the addition period (one hour); during the subsequent two-hour period of stirring, it was necessary to supply heat to maintain a refluxing temperature. This mixture was then hydrolyzed with 200 ml. of 3.6 *M* hydrochloric acid and the ether layer washed with distilled water and dried over calcium sulfate.

 TABLE II
 DISTILLATION OF FRACTIONS

Fraction	B.p., °C. (15 mm.)	Weight, g.
1	93–150	1.15
2	150–155	2.00
3	155–160	2.70
4	160–169	16.60
5	169–175	7.25
6	175–205	..

Fraction 2 crystallized in the condenser. By recrystallization was isolated 0.62 g. of biphenyl (m.p. 67–68°), free of

(3) H. C. Brown and E. A. Fletcher, *THIS JOURNAL*, **73**, 2808 (1951).

boron as evidenced by the fact that it burned without showing any green in the flame.

Fractions 3-5 were all liquids, and fraction 6, mainly triphenylborine, was a solid. All portions were diluted with equal volumes of ether and saturated with ammonia gas. A heavy white precipitate formed in all cases. The filtrates then again were saturated with ammonia to complete the precipitation. When it was necessary to treat a given fraction three or four times with ammonia to obtain complete precipitation, the volumes were maintained constant by suitable additions of ether. The ammonia complex isolated from fraction 2 (after removal of the biphenyl) amounted to 0.75 g., and the total weight of the complex obtained from 2-5 was 16.9 g. (23% yield calculated as ammonia isobutyl diphenylborinate). This material melted with evolution of ammonia at 64-67° and decomposed rapidly in benzene solution at about 70°. After standing for several weeks it became slightly discolored and the odor of butyl alcohol was noticeable. Since it decomposed so readily, no attempt was made to obtain an absolutely pure sample; however, the carbon hydrogen analysis was not far off from the value calculated for ammonia butyl diphenylborinate.

*Anal.*⁴ Calcd. for C₁₆H₂₂ONB: C, 75.4; H, 8.67. Found: C, 74.63; H, 8.44.

The complex between triphenylborine (fraction 6) and ammonia decomposed in air at about 170-176°. It was less soluble in ether than the borinate derivative. For comparative purposes, since some butyl benzeneboronate may have been present in the original mixture, it is interesting to note that the boronate esters do not precipitate with ammonia under these conditions. Thus, neither *n*-propyl nor *n*-butyl benzeneboronate could be precipitated from ether solution by ammonia. After evaporation of the ether, however, they did form a white solid with ammonia which decomposed with liberation of ammonia at about 30°.

Ammonia Butyl Diphenylborinate.—Since the yield of the borinate was rather low for the reaction run under the conditions described by König and Scharrnbeck, several variations in the reaction conditions were explored in hope that the yield could be improved.

Phenylmagnesium bromide (0.394 mole) in 420 ml. of ether was added very slowly to a solution of 45.6 g. (0.198 mole) of tri-*n*-butyl borate in 500 ml. of ether maintained at about -60°. No precipitate formed. After standing at room temperature overnight the solution was hydrolyzed with dilute hydrochloric acid. Distillation of the ether layer left a residue which was mixed with 10 ml. of *n*-butyl alcohol and 700 ml. of toluene and then distilled. The purpose of this latter step was to convert the organoboric acids to the corresponding butyl esters, which were then partially separated by distillation. Each fraction was then diluted with an equal volume of ether and the borinate ester was precipitated with ammonia gas as described in the previous experiment.

TABLE III
DISTILLATION DATA AND THE WEIGHTS OF THE AMMONIA COMPLEXES

Fraction	B.p., °C. (1 mm.)	Wt. of fraction, g.	Wt. of NH ₃ adduct, g.
1	70-125	10.45	2.34
2	125-137	28.52	22.56
3	137-165	3.08	0.53

The total amount of ammonia butyl diphenylborinate (24.9 g. from fractions 1 and 2) corresponds to a crude yield of 49%. As fraction 3 was small it is apparent that little triphenylborine had been formed in this reaction. The ammonia complex obtained from fraction 3 was the complex of triphenylborine.

In connection with this experiment it was of interest to know how much benzeneboronic acid had been formed in the reaction. As a means of separating this compound from traces of the diphenylboron compounds, the filtrates from fractions 1, 2 and 3 were distilled with ethylene glycol and toluene. Ethylene benzeneboronate (10.41 g., 18% yield) distilled at 84-91° (5 mm.). Benzeneboronic acid, m.p. 215-216°, was formed when this ester was shaken with water.

(4) The C, H and N analyses were made by H. Beck and V. Stryker.

A similar reaction between 1.84 mole of phenylmagnesium bromide and 0.92 mole of ethylene *n*-butylborate gave a 49% yield of ammonia butyl diphenylborinate and an 11% yield of ethylene benzeneboronate. From another reaction between 0.292 mole of phenyllithium and 0.146 mole of butyl ethylene borate was obtained a 41% yield of the borinate ester and a 13% yield of the ethylenebenzeneboronate.

Aminoethyl Diphenylborinate.—Ammonia isobutyl diphenylborinate (2.13 g.) was heated with 2 ml. of ethanolamine in 100 ml. of toluene. Toluene and its azeotropes were distilled until the volume was about 10 ml. On cooling, the ethanolamine ester (1.67 g., 89%) crystallized out; m.p. 187-188°. Alternately, this ester could be prepared by direct precipitation from alcohol-water. Thus, a solution of 13.70 g. of the ammonia complex in 100 ml. of ethanol and 200 ml. of water, when mixed with 6 ml. of ethanolamine in 6 ml. of water yielded 10.97 g. (91%) of the aminoethyl ester, m.p. 186-187°. This compound could be recrystallized well from alcohol and water; m.p. 189-190°. Triphenylborine does not form solid complexes with ethanolamine under these conditions.

*Anal.*⁵ Calcd. for C₁₄H₁₈ONB: B, 4.807; C, 74.70; H, 7.16; N, 6.23. Found: B, 4.795, 4.807; C, 74.02; H, 7.11; N, 6.47.

The equivalent weight of this ester, determined by a potentiometric titration with hydrochloric acid, was found to be 225, and the molecular weight, determined by the depression in the melting point of camphor, was 228. The equivalent weight and molecular weight calculated for aminoethyl diphenylborinate are 225.1.

For further characterization, a 0.2321-g. portion of the aminoester, dissolved in 10 ml. of methanol and 1 ml. of water, was mixed with 0.7491 g. of mercuric chloride and titrated with standard sodium hydroxide. On the assumption that the mercuric chloride reacted quantitatively to give phenylmercuric chloride and hydrogen chloride, one would expect to obtain one mole of hydrochloric acid and one mole of ethanolamine hydrochloride per mole of the borinate. Actually a sharp break in the titration curve did correspond to the titration of a mole equivalent of hydrochloric acid, and to an equivalent weight of the ester of 237 (calculated 225). Phenylmercuric chloride, weight 0.7 g., m.p. 252-253°, precipitated from this solution and was separated by filtration.

Diphenylborinic Anhydride.—A solution of aminoethyl diphenylborinate (5.33 g.) in a solution of methanol and acetone was acidified with hydrochloric acid. Sufficient water was added to cause the separation of layers, then the borinic acid was extracted with ether, dried with magnesium sulfate, and vacuum distilled. The distillate, 2.11 g., b.p. 210-213° (1 mm.), solidified (the major portion melted at 104-105°), but it formed an oil when added to water. The neutralization equivalent of the solid anhydride determined by titration with standard base in the presence of mannitol was 340; that calculated for diphenylborinic anhydride, 346.

Reaction of *p*-Bromophenylmagnesium Bromide with Butyl Ethyleneborate.—The Grignard reagent prepared from 7.29 g. (0.3 mole) of magnesium turnings and 70.77 g. (0.3 mole) of *p*-dibromobenzene consisted of two layers, with the upper and lower layers containing 0.116 and 0.141 mole of magnesium by titration, respectively. These two layers were added slowly with stirring to 18.38 g. (0.127 mole) of *n*-butyl ethyleneborate in 600 ml. of ether maintained at -60°. The next morning the mixture was hydrolyzed, esterified and distilled as in the previous cases. The weights of the fraction boiling at 144-172°, 172-191°, 191-195° and 195-197° at 2 mm. were 7.50, 2.87, 13.23 and 2.53 g., respectively. Redistillation of fractions 1 and 2 with ethylene glycol and toluene yielded 4.55 g. (8.2% yield) of ethylene *p*-bromobenzeneboronate, b.p. 150-153° (15 mm.), m.p. 72-80°. A small portion of this ester was converted to the free acid by heating it with water; m.p. of the acid, 254-256°. The melting point previously reported for this acid was 266°.^{2c}

Fraction 3 (11.38 g. was used) was dissolved in 1 *N* sodium hydroxide. After this solution had been extracted with ether the organic acids were liberated by addition of hydrochloric acid and then taken up in ether. Distillation of the ether left the organoboron compounds as a residue which would not crystallize. This material was then dis-

(5) We are grateful to J. M. Thoburn and Professor D. D. DeFord for the boron analyses.

solved in toluene (500 ml.) and precipitated by the addition of 5 ml. of ethanolamine; weight of the ethanolamine ester of the borinate, 6.95 g. (17% yield), m.p. 235–240°. Recrystallization of 5.14 g. of this ester yielded 4.38 g. of purified material, m.p. 236–237°.

*Anal.*⁵ Calcd. for C₁₄H₁₄ONBr₂B: B, 2.826; equiv. wt., 383. Found: B, 2.90; equiv. wt. (by titration with hydrochloric acid), 382.

The solution from the acid titration (acetone–water solution) was extracted with ether. The organic material thus obtained melted at 82–84° after recrystallization from petroleum heptane. The melting point previously reported for bis-*p*-(bromophenyl)borinic acid was 113°. ^{2b}

Diethanolamine Esters of Arylboronic Acids.—These esters were formed readily by the reaction of diethanolamine with an arylboronic acid. They are high melting solids and can serve as derivatives of the boronic acids.

A mixture of 12.20 g. of benzenboronic acid, 10.84 g. of

diethanolamine and 800 ml. of toluene was distilled until the volume of the solution was about 400 ml. After cooling, the precipitate was collected and washed with dry ether; weight 18.96 g., m.p. 212–214°. A portion (7.12 g.) was dissolved in 50 ml. of hot ethanol and reprecipitated by addition of ligroin; weight 6.10 g. (85%), m.p. 214–215°. The molecular weight of this material determined by the Rast method was over 600.

The derivatives of *p*-bromobenzenboronic acid and *p*-methoxybenzenboronic acid were prepared similarly. In the case of naphthalenboronic acid, the diethanolamine derivative was sufficiently insoluble that it could be precipitated directly from an alcohol–water solution. Thus, the addition of 3 ml. of diethanolamine in 3 ml. of water to a solution of 4 g. of naphthalenboronic acid in 10 ml. of alcohol and 5 ml. of water yielded 4.94 g. (88%) of the derivative.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY OF THE HEBREW UNIVERSITY, HADASSAH MEDICAL SCHOOL]

ω -Fluoroacetophenone. II.¹ Substitutions in the Fluoromethyl Group of ω -Fluoroacetophenone

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Only one hydrogen atom of the fluoromethyl group of ω -fluoroacetophenone can be substituted by halogens. Nucleophilic reagents replace only the second halogen in the disubstituted acetophenones, but leave the fluorine atom untouched. The new halogen derivatives are all powerful lachrymators.

Since fluorine possesses the highest electronegativity among all elements but does not exert any appreciable steric interference with other substituents, it appeared of interest to study substitution reactions of the fluoromethyl group of ω -fluoroacetophenone (I). This ketone does not react with elementary chlorine under conditions which permit an almost quantitative chlorination of acetophenone itself. Likewise, N-chlorosuccinimide was without effect, but in the presence of benzoyl peroxide in boiling carbon tetrachloride a trace of lachrymatory material was formed. Gryszkiewicz-Trochimowski³ achieved chlorination of fluoroacetyl chloride by sulfuryl chloride in a closed vessel at 150–160° and obtained about 50% yield of the monochloro derivative. We have observed that a solution of I in sulfuryl chloride undergoes a spontaneous reaction at room temperature. Gas evolution sets in after an induction period of about 30 min and stops after 15–16 hours. From this mixture α -chloro- α -fluoroacetophenone (IIa) can be isolated in 75% yield. Peroxide has no influence on the speed or yield of this reaction. The chlorination of I thus can be considered as an electrophilic substitution, but the curious role of sulfuryl chloride is not understood.

In view of these results it is surprising that bromination of I can be accomplished with elementary bromine in ether in presence of a catalytic amount of aluminum chloride. The yield of α -bromo- α -fluoroacetophenone (IIb) was almost quantitative. On the other hand, no reaction is observed with io-

dine or its monochloride. The iodo derivative (IIc) was prepared by halogen exchange between IIa or b and potassium iodide in ethanol, in analogy to the method applied by Swarts⁴ to the synthesis of ethyl iodofluoroacetate. In this series only the halogen beyond fluorine can be removed by direct electrophilic substitution, whereas, *e.g.*, in α,α -dibromoacetophenone both halogens are exchangeable.⁵

The direct replaceability of *one* halogen only in the ketones IIa–c was demonstrated in other examples also. Thus, with ammonium thiocyanate, α -fluoro- α -thiocyanoacetophenone (II_d) was formed and with trimethylamine the quaternary ammonium salt III. However, with other nucleophilic reagents, complicated secondary reactions took place, which will be reported in a future publication.

The facile introduction of *one* additional halogen atom into the fluoromethyl group of I contrasts sharply with the resistance of compounds IIa–c toward further halogenation. They were not attacked by boiling sulfuryl chloride or by bromine under a variety of experimental conditions, although α,α -dichloro- or dibromoacetophenone can be halogenated further.⁶ This might give the impression that only one hydrogen atom of the –CH₂F– group could be substituted. However, condensation with benzaldehyde produces α -fluorobenzalacetophenone (IV) in 40% yield.

The fluorine atom in the ketones IIa–d is, however, not entirely inert. Thus they all give the same dioxime of m.p. 172°⁷ and the same bis-semicarba-

(1) Part I. F. Bergmann and A. Kalmus, *THIS JOURNAL*, **76**, 4137 (1954).

(2) Part of a Ph.D. thesis, submitted to the Hebrew University, 1955.

(3) E. Gryszkiewicz-Trochimowski, A. Sporzynski and J. Wuuk, *Rec. trav. chim.*, **66**, 413 (1947).

(4) F. Swarts, *Memoires couron., Acad. roy. Belg.*, 61 (1903); *Chem. Zentr.*, **74**, 1, 11 (1903).

(5) A. Collet, *Bull. soc. chim.*, [3] **23**, 830 (1900).

(6) J. G. Aston, J. D. Newkirk, J. Dorsky and D. M. Jenkins, *THIS JOURNAL*, **64**, 1413 (1942).

(7) A. Russanow, *Ber.*, **24**, 3500 (1891).