zinc, and 5 parts of concd. hydrochloric acid was boiled for twenty-four hours. The butyric acid was purified conveniently by recrystallization of its sodium salt from water. The free acid may be purified by sublimation.

[55] I. A mixture of 1 g. of No. 40, 3 cc. of concd. sulfuric acid, and 1 cc. of water was heated at 100° for one hour. When the reaction mixture was poured into water, a crystalline precipitate formed, which was dissolved in ether. The ether solution was extracted with dilute alkali, and yielded on evaporation 0.7 g. of practically pure ketone. For further purification the ketone may be recrystallized from alcohol or sublimed in an oil-pump vacuum.

II. A mixture of 1 g. of dodecahydrotriphenylene (prepared according to Mannich) and 1 g. of chromic acid in 2 cc. of 80% acetic acid was allowed to stand at room temperature for five hours and then poured into water. The precipitated ketone was purified by recrystallization from alcohol and by vacuum sublimation, m. p. 221.5–222.5°. The mixed melting point with the ketone obtained by ring closure of the octahydrophenanthrylbutyric acid was 221–222°. (The mixed m. p. with dodecahydrotriphenylene was 214–217°.)

A mixture of 1 g. of No. 41, 5 g. of amalgamated zinc, and 5 cc. of concd. hydrochloric acid was boiled under reflux for eighteen hours. The hydrocarbon was isolated as a white crystalline mass and melted, after vacuum sublimation, at 226–228°. Dodecahydrotriphenylene prepared according to Mannich[8] melts, after crystallization from ethanol and vacuum sublimation, at 226–229°.

Summary

A number of scattered and disconnected experiments in the phenanthrene series is described.

These experiments include the preparation of amides and β-amino ethyl esters of phenanthroic acids, the preparation of amino alcohols of the type $C_{14}H_9CHOHCH_2NR_2$ and the synthesis of 4-ketododecahydrotriphenylene.

UNIVERSITY, VIRGINIA RECEIVED APRIL 4, 1938

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

A Convenient Preparation of Volatile Acid Chlorides

BY HERBERT C. BROWN

The usual procedure for the preparation of organic acid chlorides involves the action of an inorganic acid chloride upon an organic acid. Among the chlorides which have been used are silicon tetrachloride, the sulfur chlorides, phosphorus tri- and pentachlorides, and thionyl chloride. However, only the phosphorus chlorides and thionyl chloride have been widely adopted in the laboratory.

The possibility of utilizing organic acid chlorides for the preparation of other acid chlorides has been neglected for the most part. Adams and Ulich[1] have reported that they could obtain almost quantitative yields of acid chlorides by the action of oxalyl chloride on organic acids. The cost and instability of the reagent, however, preclude the general adoption of this procedure. Van Dorp and Van Dorp[2] found that they could obtain fumaryl chloride by the action of phthalyl chloride on fumaric acid. This method has been extended lately by Kyrides,[3] who confirms the above preparation and reports the preparation of butyryl chloride in 90% yield. Further, the action of chloroacetyl chloride on acetic acid has been utilized for the preparation of acetyl chloride.[4]

In the course of an investigation now being conducted the need for a large number of volatile acid chlorides led to the development of a simple procedure for their preparation, involving the action of a relatively slightly volatile acid chloride upon an organic acid. Because of its cheapness and availability, benzoyl chloride was selected as the non-volatile acid chloride. The procedure is very simple: the acid is mixed with an excess of benzoyl chloride and the acid chloride desired is distilled through a small column directly out of the reaction mixture. The reaction is general, limited only by the volatility of the acid chloride—it has given excellent results with all the lower fatty acids, saturated, unsaturated, and their halogen derivatives, which have been tested.

Other advantages of the new method are its rapidity (an average preparation can be completed in one hour) and its economy (benzoyl chloride is much cheaper than either thionyl chloride or phosphorus pentachloride). If it is desired, benzoic acid can be recovered easily in high yield from the residue.

Experimental

1. **Apparatus and Materials.**—The fractionating column used was 25 cm. in length. The inner tube (9 mm.) was packed with a spiral containing 2 turns per cm. made from no. 18 tantalum wire. The flasks were fitted to the

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(1) Adams and Ulich, THIS JOURNAL, **42**, 599 (1920).

(2) Van Dorp and Van Dorp, *Rec. trav. chim.*, **25**, 96 (1906).

(3) Kyrides, THIS JOURNAL, **59**, 206 (1937).

(4) U. S. Patent 1,850,205 (1932).

column by means of standard ground glass joints. To reduce loss of acid chloride by the hydrogen chloride evolved, the receiver was immersed in a freezing mixture during the preparation of the more volatile acid chlorides.

The acids used were Eastman Kodak Company chemicals unless otherwise specified. The dichloroacetic acid was the practical grade and was purified by recrystallization of the aniline salt.[5] *n*-Caproic acid was prepared by the malonic ester synthesis[6] and both *n*-valeric acid[7] and trimethylacetic acid[8] were prepared by the Grignard synthesis. Isobutyric and isovaleric acids were obtained by the oxidation of the corresponding alcohols.[9]

2. **General Procedure.**—In the round-bottomed flask surmounted by the fractionating column is placed 0.25 mole of the acid and 0.375 mole of benzoyl chloride. The mixture is heated strongly until it begins to boil, and then the acid chloride is distilled out of the reaction mixture as rapidly as is consistent with good separation from the other constituents in the flask. This can be accomplished by distilling at a rate such that the temperature at the top of the column does not exceed the boiling point of the acid chloride. Usually the temperature registered will be several degrees below the true boiling point, due to the fact that the acid chloride is partially carried over by the hydrogen chloride given off by the reaction mixture. If the preparation has been carried out correctly, the distillate is practically pure acid chloride containing a small amount of dissolved hydrogen chloride. For most purposes this material can be used directly. However, the yields recorded in this paper are based upon the pure refractionated material.

Although the best yields were obtained with the apparatus described above, a modified Claisen flask has been used in several experiments with but little decrease in yield. In refractionating the distillate care should be taken to maintain a very high reflux ratio at first; otherwise the dissolved hydrogen chloride tends to carry over a considerable amount of the acid chloride below its true boiling point.[10]

3. **Determination of Conditions for Maximum Yield.**—Preparations were carried out with propionic, butyric, and monochloroacetic acids using varying amounts of benzoyl chloride with and without a slow stream of hydrogen chloride (Table I). In the experiment using hydrogen chloride a slow stream of the carefully dried gas was bubbled through the reaction mixture for the duration of the distillation.

TABLE I

Acid	Ratio of benzoyl chloride to acid[a] 2:1	3:2	1:1	1:1 + HCl
Propionic	89%[b]	84%	63%	70%
Butyric	87	80	54	66
Monochloroacetic	76	71	45	52

[a] 0.25 mole of acid was used in each case.

[b] Yield of acid chloride calculated on the basis of the amount of acid used.

The use of the stream of hydrogen chloride increased the yield but slightly and in view of the extra labor involved the practice is not recommended. The use of an excess of benzoyl chloride, either in the molar ratio 2:1 or 3:2 is a much more satisfactory means for improving the yield.

The influence of the rate of distillation of the acid chloride is to be noted in the following result. Using benzoyl chloride and propionic acid in a molar ratio of 3:2 and keeping all conditions constant except the rate of distillation, the yield was raised from 75 to 84% as the rate of distillation was increased.

The experimental results are summarized in Table II. In order to emphasize the advantages offered by benzoyl chloride as a reagent for the preparation of volatile acid chlorides over those reagents (PCl_5, PCl_3, $SOCl_2$) which have been

TABLE II

SUMMARY OF EXPERIMENTAL RESULTS

Acid	Boiling range, °C.	1 mole acid +1.5 mole C_6H_5COCl yield, %[a]	1 mole acid +2.0 mole C_6H_5COCl yield, %[a]
Acetic	48–51	88	85
Monochloroacetic	105–107	71	76
Dichloroacetic	105–107		73
Trichloroacetic[b]	116–119	51	56
Propionic	77–78.5	84	89
n-Butyric	101–102.5	80	87
Isobutyric	91–93	82	88
n-Valeric	125–127	76	84
Isovaleric	114–116		84
Trimethylacetic	103–104	79	92
Caproic	150–153		80
Crotonic	120–123	72	80

[a] The yield is based on the pure refractionated material. Since the yield in these preparations (using 0.25 mole of acid) was 20–30 g. and the column holdup was approximately 1.5–2.0 cc., the yields should be considerably increased in larger preparations. To test this point, and to determine the feasibility of larger scale preparations, 1.5 moles of propionic acid (111 g.) was treated with 2.25 moles of benzoyl chloride (316 g.). The yield of propionyl chloride was 92% (128.2 g.). [b] In the preparation of trichloroacetyl chloride a relatively large amount of low boiling distillate was obtained. Investigation disclosed the presence of both chloroform and carbon tetrachloride. The chloroform evidently arises from the thermal decomposition of trichloroacetic acid. The source of the carbon tetrachloride must be the little-known reaction $CCl_3COCl \longrightarrow CCl_4 + CO$ [Böeseken, *Rec. trav. chim.*, **29**, 112 (1910)]. This latter reaction also takes place with dichloroacetyl chloride and it may offer a convenient means of preparation of compounds of the type $RCCl_3$, $RCCl_2Br$, etc. The reaction will be investigated further.

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(5) Doughty and Black, THIS JOURNAL, **47**, 1091 (1925).

(6) *Org. Syntheses*, **16**, 62, Note 6 (1936).

(7) *Ibid.*, Coll. Vol. I, p. 355, Note 10.

(8) *Ibid.*, p. 510.

(9) Pierre and Puchot, *Ann. chim. phys.*, [4] **28**, 363 (1873).

(10) Checkers had difficulty confirming the yields and boiling ranges recorded in Table II until this precaution was stressed.

commonly utilized for this purpose, the results of a recent study of the preparation of acid chlorides[11] will be summarized. Thionyl chloride gives poor yields of acid chlorides in the case of the lower aliphatic acids, averaging less than 50%. The halogen-substituted acetyl chlorides can be produced only after long refluxing, often in poor yield. For example, Clark and Bell report that they obtained a 12% yield of trichloroacetyl chloride after sixty-six hours of refluxing. Phosphorus pentachloride cannot be applied to the production of many acid chlorides whose boiling points are too close to that of phosphorus oxychloride to be readily separable. Phosphorus trichloride has a similar disadvantage—phosphorous acid often can be separated from the desired acid chloride only with great difficulty.

4. Recovery of Benzoic Acid.—One quarter mole each of propionic acid and benzoyl chloride was treated by the general procedure. The reaction residue was poured into 700 cc. of water and the mixture was boiled. To aid in the solution of some oily material (probably benzoic anhydride) a little sulfuric acid was added and the mixture was boiled for two hours. Upon cooling, benzoic acid was recovered in 91% yield, quite pure (m. p. 120–121.5°).

Mechanism of the Reaction

It is usually assumed that when an acid chloride acts upon an acid, the reaction takes the following course[12]:

$$\begin{tikzcd}
\mathrm{RCOCl} + \mathrm{R'COOH} \arrow[r, shift left] & \mathrm{RCOOCOR} + \mathrm{HCl} \arrow[l, shift left] \arrow[d, shift left] & \\
& \mathrm{RCOOH} + \mathrm{R'COCl} \arrow[u, shift left] & \mathrm{A}
\end{tikzcd}$$

Supporting this view is the fact that acid anhydrides can be prepared by refluxing an equimolar mixture of an acid and an acid chloride, or by removing the hydrogen chloride by other means, such as an added base like pyridine.[13] On the other hand, it seems unlikely that such high yields as the procedure recommended here has given could have been obtained if the splitting off of hydrogen chloride is a necessary step in the formation of the acid chloride R'COCl. If this were the case, in view of the relatively high temperature of the reaction mixture, the loss of hydrogen chloride from the system and the consequent decrease in yield would be expected to be much greater than actually occurs.

Therefore, it appears likely that the formation of the acid chloride takes place either directly, as

$$\mathrm{R{-}COCl} + \mathrm{R'COOH} \rightleftarrows \mathrm{RCOOH} + \mathrm{R'COCl} \qquad \mathrm{B}$$

or indirectly through some intermediate product which does not involve the complete separation of hydrogen chloride. If this is the case, then, in the preparation, (A) represents the side reaction to which is due the evolution of hydrogen chloride; and the improvement of the yield with rapid distillation can be explained on the ground that the sooner the acid chloride is removed from the reaction mixture the less chance it has to participate in this side reaction.[14]

It might be thought that a study of the reaction of acid chlorides with esters might solve the problem of the mechanism

$$\mathrm{RCOCl} + \mathrm{R'COOR''} \longrightarrow \mathrm{RCOOCOR'} + \mathrm{R''Cl} \quad (\mathrm{A'})$$
$$\mathrm{RCOCl} + \mathrm{R'COOR''} \rightleftharpoons \mathrm{RCOOR''} + \mathrm{R'COCl} \quad (\mathrm{B'})$$

However, the experimental data recorded in the literature are contradictory. For example, Döbner[15] reported that benzoyl chloride reacts with phenyl acetate in the presence of a trace of zinc chloride to produce phenyl benzoate and acetyl chloride.

$$\mathrm{C_6H_5COCl} + \mathrm{CH_3COOC_6H_5} \longrightarrow \mathrm{C_6H_5COOC_6H_5} + \mathrm{CH_3COCl}$$

This supports mechanism B'. On the other hand, Kyrides[16] has reported that ethyl benzoate and benzoyl chloride react in the presence of zinc chloride at moderately high temperatures to give fair yields of benzoic anhydride and ethyl chloride (mechanism A'). Further confusing the problem is the recent claim that the yield of alkyl chlorides in the reactions of acid chlorides with a number of esters is small or non-existent. When an alkyl chloride is formed, it appears that the corresponding unsaturated hydrocarbon is an intermediate.[17]

On the basis of this evidence it is impossible to draw any definite conclusion as to the mechanism of this reaction. However, investigation into this problem has been undertaken and it is hoped that results may soon be available to clear up this question.

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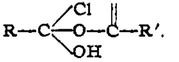
[11] Clark and Bell, *Trans. Roy. Soc. Can.*, III, **27**, 97 (1933).

[12] Groggins, "Unit Processes in Organic Synthesis," McGraw-Hill Book Co., Inc., New York, N. Y., 1935, p. 151.

[13] Wedekind, *Ber.*, **34**, 2070 (1901).

[14] Dr. Weldon Grant Brown has called the writer's attention to the fact that both anhydride and acid chloride formation may take place through the formation of the same intermediate 

$\mathrm{R{-}C(Cl)(OH){-}O{-}C({=}O){-}R'}$. In this connection it is interesting to note that stable addition products of both acids and acid chlorides to carbonyl groups have been recorded [Meyer and Dulk, *Ann.*, **171**, 65 (1874), and Schiff, *ibid.*, **154**, 347 (1870), footnote].

[15] (a) Döbner, *ibid.*, **210**, 255 (1881); (b) Bodroux, *Bull. soc. chim.*, [3] **23**, 54 (1900).

[16] Kyrides, THIS JOURNAL, **55**, 4630 (1933).

[17] Amitin and Hirshberg, *C. A.*, **31**, 6610 (1937).

Summary

1. A simple general procedure for the preparation of volatile acid chlorides is described, involving the distillation of the desired acid chloride from a mixture of benzoyl chloride and an organic acid.
2. The procedure has been used in the preparation of twelve aliphatic acid chlorides with yields of 70–90%.
3. The mechanism of the reaction is discussed. No definite conclusions concerning the mechanism could be reached.

CHICAGO, ILLINOIS RECEIVED MARCH 24, 1938

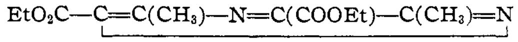
[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

A Synthesis of *dl*-Threonine

BY HOMER ADKINS AND E. WILKINS REEVE[1]

Rose and associates, after isolating *dl*-threonine from the hydrolysate of fibrin, showed the compound to be one of the stereoisomeric α-amino-β-hydroxybutyric acids.[2] West and Carter have synthesized these acids by adding mercuric acetate to crotonic acid in methanol, then brominating the product to give $CH_3CH(OCH_3)CHBr\text{-}COOH$. The latter compound was then ammonolyzed and hydrolyzed to $CH_3CHOHCHNH_2\text{-}COOH$.[3]

It appeared that the α-amino-β-hydroxybutyric acids could be made by nitrosating acetoacetic ester and then hydrogenating the resulting oximino-acetoacetic ester. However, when Winans[4] attempted to do this he obtained a pyrazine,



$$EtO_2C—C{=}C(CH_3)—N{=}C(COOEt)—C(CH_3){=}N$$

The formation of a pyrazine in the hydrogenation of an α-oximino ketone probably involves the reaction of an imino group. Whether an imine is formed in the hydrogenation of an oxime depends upon whether the first mole of hydrogen cleaves the oxygen to nitrogen linkage to give $R_2C{=}NH$, or adds to the carbon to nitrogen double bond to give $R_2CHNHOH$. There is evidence that the first reaction with an oxime is hydrogenolysis rather than hydrogenation. It seemed possible that if the ether, $R_2C{=}NOEt$, rather than the oxime were submitted to hydrogenation, the order of these reactions would be reversed.[5] Therefore the ethyl ether of α-oximino-acetoacetic ester was prepared and submitted to hydrogenation over Raney nickel. The reaction proceeded smoothly and rapidly to give ethyl α-amino-β-hydroxybutyrate without the formation of a detectable amount of the pyrazine.

The practicality of the method outlined above is indicated by the following facts. Acetoacetic ester was converted in over 65% yield to oximino-acetoacetic ester. The oximino ester was ethylated with diethyl sulfate to give a 40% yield of the ether, $CH_3C(O)C{=}(NOEt)COOEt$. The ether was hydrogenated within twenty minutes at 90–100°. The resulting hydroxyamino ester may be isolated by distillation, but better yields of the desired acids were obtained by hydrolyzing with boiling water the product of hydrogenation. The yield of α-amino-β-hydroxybutyric acids was 75%. The *dl*-threonine, m. p. 228°, then may be separated in over 50% yield from the stereoisomeric *dl-allo*-threonine, m. p. 252°, through the use of water and alcohol.

After the completion of the experiments referred to above, it was discovered that the proportions of products to be obtained by the hydrogenation of oximino-acetoacetic ester over Raney nickel, were determined by the pressure of hydrogen. For example when a hydrogenation was carried out at an initial pressure of 120 atmospheres, 2.2 moles of hydrogen per mole of oximino-acetoacetic ester was absorbed within about fifteen minutes, while with an initial pressure of 320 atmospheres, 2.8 moles of hydrogen was absorbed within ten minutes. These time intervals refer to the period from the beginning of a reasonably rapid hydrogenation, at about 40°, to the completion of reaction at about 70°. Similar comparisons were made for a maximum temperature of 80 and 90°.

The product isolated from the hydrogenation at the lower pressure was a pyrazine as observed by Winans. However, when the reaction product

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[1] This investigation was supported in part by a grant from the Wisconsin Alumni Research Foundation.

[2] McCoy, Meyer and Rose, *J. Biol. Chem.*, **112**, 283 (1935); Meyer and Rose, *ibid.*, **115**, 721 (1936).

[3] West and Carter, *ibid.*, **119**, 103 (1937).

[4] Winans and Adkins, THIS JOURNAL, **55**, 4169 (1933).

[5] Jones and Major [*ibid.*, **52**, 669 (1930)] obtained O-alkyl substituted hydroxylamines hydrochloride by the hydrogenation of O-alkyl substituted oximes over Adams platinum catalyst.