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# Condensations by Sodium. V. Preparation of Acids. Dicarboxylic Acids from Monohalogen Compounds

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In further study[1] of the preparation of acids by interaction of sodium, organic halides, and carbon dioxide the syntheses of benzoic, *m*-toluic, *p*-toluic and *p*-phenylbenzoic acids from the corresponding chlorides have been accomplished with yields of 78, 88, 95 and 67%, respectively. *o*-Chlorobenzaldehyde has also been found to yield 47% of *o*-phthaldehyde acid despite the fact that it has another group which might be attacked by the sodium. All of these chlorides reacted readily under pressures of carbon dioxide varying from 40 to 600 pounds in benzene as a solvent. An exceedingly interesting part of the research arose when the reaction with *n*-amyl chloride was tried. In addition to the expected caproic acid, large quantities of butylmalonic acid were found among the products. The presence of this dicarboxylic acid could not be ascribed to impurities in the technical amyl chloride used for amyl chloride prepared from interaction of amyl alcohol, zinc chloride and hydrochloric acid behaved similarly. In all cases the quantity of butylmalonic acid far exceeded the amount which could have been due to the presence of any dichloride and was usually greater than the yield of caproic acid. The conclusion must be drawn that a mono-halogen compound yielded a dicarboxylic acid as a major product of its reaction with sodium and carbon dioxide.

The synthesis of the malonic acid occurred exothermally in ligroin with surprising ease. Pressure, solvent and the relative quantities of sodium and amyl chloride influenced the proportion of each product formed. In general at low pressures, for example up to 100 pounds, the Wurtz reaction predominated; around 200–400 pounds malonic acid was formed in quantity; at still higher pressures oxalic and carbonic acids were the major products (see Table III). The process is a general one for primary and secondary chlorides. In Table IV there is given a summary of the results obtained for a number of aliphatic chlorides under conditions which were favorable for the formation of butylmalonic acid but not necessarily best suited for the preparation of other dicarboxylic acids. The yield of the malonic acid—butylmalonic acid as an example—was calculated on the basis that equation 1 pictured the correct consumption of reagents.

$$2C_5H_{11}Cl + 4Na + 2CO_2 \longrightarrow C_5H_{12} + C_4H_9CH(COONa)_2 + 2NaCl \quad (1)$$

Similar equations may be written for the formation of the other malonic acids. The occurrence of the monocarboxylic acids among the products is represented by equation 2. The percentage of

$$RCl + 2Na + CO_2 \longrightarrow RCOONa + NaCl \quad (2)$$

oxalic acid was based on the quantity of sodium used on the assumption that its formation was expressed by equation 3. Some carbonate was also

$$2CO_2 + 2Na \longrightarrow (COONa)_2 \quad (3)$$

formed which we assumed involved no consumption of organic halide, since carbon has been shown[2] to result from the action of carbon dioxide on sodium at 350°. Satisfactory agreement was found between the above equations and material balances in which the quantities of all major products except pentane and decane were measured. Since no organic chloride is concerned in the formation of oxalic acid, the yields of acids in the table are given first on the basis of the sodium consumed and second on the amount of organic chloride used. The latter was obtained by calculation from titration of the chloride ion.

Although ligroin was a very satisfactory solvent for the reaction with the alkyl chlorides, benzene also was tried. The products in this case were even more varied for tere- and isophthalic were found in addition to caproic and butylmalonic acids. This solvent participation is being studied further. Experiments are also being carried out which may give information on the mechanisms by which the reactions occur.

## Experiments

**Aromatic Chlorides** (with W. J. L.).—An Adkins[3] high pressure apparatus, although more than sufficient for the pressure requirements of the reaction, provided a welcome factor of safety in the early stages of this work. The

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[1] For previous work in this series see Morton and Stevens, This Journal, **53**, 4028 (1931).

[2] Chands and Roman, *Compt. rend.*, **192**, 1381 (1931).

[3] Adkins, Cramer and Connor, This Journal, **53**, 1402 (1931). Purchased from the Burgess–Parr Company.

usual order was first to put the benzene and sodium sand (made by shaking in xylene solution) in the bomb, then to add solid carbon dioxide for cooling the mixture and rendering the sodium temporarily inert, and finally to introduce the halide. After closing and inserting the container in the apparatus, carbon dioxide was admitted until the desired pressure was constant under shaking. Heat was then applied. Upon the conclusion of the reaction the bomb was allowed to cool, the contents poured out and treated with a little alcohol to decompose the sodium, and the liquid extracted with water from which the acid was recovered by acidification. The crude product, usually of a fair degree of purity, was dried and weighed. Table I gives the results from a series of experiments. The yield is calculated from the amount of sodium used. The pressure is that at the start of the reaction. The effect of pressure may be seen in the series of runs with chlorobenzene and *m*-chlorotoluene in both of which high pressure, other factors being constant, either decreased or prevented a yield of the corresponding acid. Negative results were obtained with α-chloronaphthalene, *o*-chlorodiphenyl, chlorocyclohexane and benzyl chloride. These compounds, although unreactive under the conditions tried, may not be entirely inert since α-chloronaphthalene when allowed to react at room temperature in ether solution with sodium for some time before carbon dioxide was added, gave rise in one experiment to about 25% of crude naphthoic acid. Experiments with *n*-amyl chloride indicated that the products were more varied than expected.

TABLE I

| Moles | Sodium sand, g. atoms | Benzene, cc. | Pressure, pounds | Max. temp., °C. | Yield g. | Yield % |
|---|---|---|---|---|---|---|
| | | | Chlorobenzene | | | |
| 0.49 | 0.213 | 50 | 600 | 103 | 0 | 0 |
| .49 | .212 | 50 | 500 | 120 | 3.0 | 22 |
| .49 | .214 | 50 | 400 | 120 | 11.4 | 78[d] |
| .49 | .22 | 50 | 350 | 115 | 9.0 | 67 |
| .49 | .22 | 50 | 300 | 110 | 9.7 | 72 |
| .49 | .174 | 50 | 200 | 122 | 7.8 | 73 |
| .49 | .22[a] | 50 | 700 | 107 | Slight | Slight |
| | | | *m*-Chlorotoluene | | | |
| 0.34 | 0.026 | 50 | 50 | 117 | 1.4 | 88[d] |
| .17 | .026 | 50 | 50 | 111 | 1.2 | 75 |
| .43 | .22 | 50 | 600[b] | 170 | 2.0 | 13 |
| .43 | .22 | 50 | 500[b] | 125 | 4.0 | 27 |
| .43 | .22 | 50 | 400[b] | 114 | 3.5 | 22 |
| .21 | .22 | 50 | 500[b] | 128 | 0.7 | 5 |
| | | | *p*-Chlorobiphenyl | | | |
| 0.042 | 0.017 | 50 | 60 | 110 | 1.1 | 65[d] |
| .085 | .017 | 100 | 40 | 111 | 1.2 | 67 |
| .085 | .017 | 100 | 80 | 120 | 1.2 | 67 |
| | | | *p*-Chlorotoluene | | | |
| 0.43 | 0.22[a] | 50 | 500 | 50 | 14.3 | 95[d] |
| | | | *o*-Chlorobenzaldehyde | | | |
| 0.18 | 0.044 | 25 | 100 | 113 | 1.5 | 47[c,d] |
| | | | *o*-Chlorotoluene | | | |
| 0.17 | 0.039 | 30 | 120 | 128 | | Slight |

[a] Small lumps of sodium used. [b] Gravel used in the bomb to aid in rubbing off any unreactive surface on the metal. [c] Not enough carbon dioxide was present to react completely with the sodium and halide. [d] The purity may be judged from the fact that the melting points of the crude acids are 118, 106, 215, 165 and 91° for the first five chlorides in the above table. The values recorded in Beilstein for the same acids are in order, 121, 110.5, 218, 176–177 and 97°. A single recrystallization was sufficient to raise the melting point to a value near that recorded.

**Aliphatic Chlorides** (with I. H.).—A special apparatus more suitable for these reactions was constructed. An iron autoclave (1500 ml. capacity) with a flanged lid was set in a large trunnion ring so that it could be suspended and shaken. The ring was constructed as follows: Iron rods were brazed onto a short section of iron pipe of the proper diameter. These rods served as pivots and worked in bearings attached to a rigid pipe stand frame. The autoclave was supported in this collar by its flange. Around the bottom of the autoclave another collar was clamped. This in turn was connected through a rod to a motor-driven eccentric. Gas heat was applied to the bottom as needed. The flanged cover was fitted with a thermometer well, gage and valve inlet.

The general procedure in carrying out a reaction was to put the sodium sand, made by mechanical stirring in hot kerosene and partially freed from solvent by decantation, into the autoclave with ligroin. The organic chloride was put into a 200-ml. beaker and set inside the bomb after which the top was bolted. Carbon dioxide was admitted until the pressure was constant at the level desired. The autoclave was then inserted in the trunnion ring described, the lower collar attached, and the contents either mixed at once or heated and mixed by shaking. The initiation of the reaction could be determined by plotting the time of heating against the temperature, or by watching the sudden jump of the galvanometer needle on the potentiometer or by observing the sudden change in pressure on the gage. When the reaction was concluded the bomb was allowed to cool. When opened the liquid and solid were poured into a beaker. If the reaction had not been too vigorous the liquid was water clear. The solid usually varied in color from a deep to a gray-blue. The presence of carbon, mud colored solid, or red liquid indicated that the reaction had been too violent. After filtering in a Büchner funnel, washing with ligroin, and drying in a vacuum oven at 80° the solid was decomposed with water.

Separation of the water soluble acid products, *i. e.*, the monocarboxylic, dicarboxylic and oxalic acids, was best effected by the use of solvents. Upon extraction of the acidified aqueous solution with ligroin the first named acid was almost completely removed. A second extraction using ether as a solvent removed the malonic acid. So nearly complete was the separation of the products of the reaction with amyl chloride that the malonic acid generally crystallized upon evaporation of the ether. A failure to recover this compound as a solid was rectified by washing the residue from the ether extraction with a little ligroin. The actual quantities of mono- and dicarboxylic acids were then determined by titration of the extracted material. Tests made of this method with mix-

TABLE II

| Amyl chloride, ml. | Ligroin, ml. | Carbon dioxide, lb. | Sodium, g. | Init. temp., °C. | Yield based on sodium, % Malonic | Caproic | Oxalic | Carbonic | Wurtz | Total | Variable observed Other factors constant |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 200 | 0 | 920 | 15 | R[a] | 17 | 20 | 23 | 27 | 17 | 104 | Change of pressure |
| 200 | 0 | 500 | 15 | R | 22 | 18 | 19 | 23 | 16 | 98 | |
| 50 | 100 | 160 | 3 | R | 32 | 35 | 7 | 17 | 11 | 102 | Change of pressure |
| 50 | 100 | 120 | 3 | R | 39 | 25 | 4 | 10 | 22 | 100 | |
| 50 | 100 | 80 | 3 | R | 21 | 18 | 2 | 5 | 42 | 88 | |
| 120 | 130 | 380 | 15 | 50 | 22 | 20 | 32 | 12 | 2 | 88 | Variation of amount of solvent |
| 120 | 70 | 380 | 15 | 50 | 26 | 21 | 22 | 24 | 5 | 98 | |
| 120 | 10 | 380 | 15 | 50 | 29 | 23 | 15 | 20 | 14 | 101 | |
| 50 | 150 | 120 | 3.0 | R | 30 | 39 | 9 | 9 | 13 | 100 | Varying quantity of solvent |
| 50 | 100 | 120 | 3.0 | R | 39 | 25 | 5 | 10 | 22 | 101 | |
| 50 | 70 | 120 | 3.0 | R | 23 | 19 | 2 | 7 | 48 | 99 | |
| 50 | 0 | 120 | 7.0 | R | 20 | 13 | 4 | 10 | 53 | 100 | Variation of amount of sodium |
| 50 | 0 | 120 | 3.5 | R | 39 | 25 | 4 | 10 | 22 | 100 | |
| 50 | 0 | 120 | 2.5 | R | 37 | 30 | 3 | 8 | 23 | 101 | |

[a] R refers to room temperature.

tures of known quantities of caproic and butylmalonic acids showed that well over 95% separation of the acids could be achieved by successive extractions with an equal volume of ligroin and of ether. The procedure is not so good with some of the homologs of these acids. The oxalic acid left in the aqueous solution could be removed by a final extraction with ethyl acetate. It could also be determined by permanganate titration. The amount of organic chloride consumed in the reaction was found by the customary titration for chloride ion of an aliquot part of the aqueous solution. Carbonic acid was estimated by first titrating an aliquot portion with phenolphthalein as an indicator; precipitating the carbonate with barium nitrate in another portion, filtering, titrating the remaining alkali as before, and calculating the carbonate content from these values. The identity of all acid products except carbonic was ascertained by boiling points or melting points and by acid equivalents. Mixed melting points were used to identify butylmalonic and oxalic acids. Thermal conversion of the malonic acids to monocarboxylic acids was likewise employed as a test. Oxalic acid was also isolated as the calcium salt and evaluated from its reducing action on permanganate.

In experiments where benzene was employed as a solvent there separated on acidification a water-soluble material. This precipitate was filtered and converted to a mixture of methyl esters which was separated by crystallization. Melting points and mixed melting points with known samples showed that the original mixture was composed of tere- and isophthalic acids. No phthalic acid was located but a fluorescein test indicated that its absence had not been demonstrated conclusively. Further experiments on the participation of the solvent in the reaction are in progress.

As a precaution against the likelihood of an effect due to an impurity a run with *n*-amyl chloride, prepared from *n*-amyl alcohol, was made. Technical *n*-amyl alcohol was first fractionated through a Davis column of 20 turns in order to obtain a fraction boiling within 1°. This alcohol was then converted to the chloride by refluxing with hydrochloric acid in the presence of zinc chloride according to the general directions of Norris.[4] The chloride so obtained was dried over calcium chloride and fractionated. A portion, 120 ml., boiling between 106 and 108° (760 mm.) was treated in 100 ml. of ligroin with sodium, 15 g., and carbon dioxide, 200 lb., at an initial temperature of 80°. The yield of butylmalonic acid was 29%. A considerable number of experiments with technical *n*-amyl chloride were made in order to discover some factors which might affect the yield of the various acids obtained in the process. The conditions and results in some selected runs are given in Table II. The yields are calculated on the sodium used. Failure of the total percentage to equal exactly 100 can be ascribed chiefly to errors in weighing sodium sand. The last column lists the variables studied.

In Table III the conditions so far found for optimum or very high yields of each of the four acids from the amyl chloride reaction are listed.

TABLE III

| Acid | Amyl chloride, ml. | Sodium, g. | Ligroin, ml. | Carbon dioxide, lb. | Init. temp., °C. | Yield, g. | Yield, based on Na, % | Rx, % |
|---|---|---|---|---|---|---|---|---|
| Caproic | 50 | 3.5 | 150 | 120 | 25 | 3.4 | 38 | 47.5 |
| Butylmalonic | 50 | 3.5 | 100 | 120 | R | 2.4 | 39[a] | 40.5 |
| Butylmalonic | 120 | 15 | 70 | 380 | 50 | 6.9 | 26 | 51[b] |
| Oxalic | 120 | 15 | 130 | 380 | 50 | 12.7[c] | 32[d] | |
| Carbonic | 120 | 15 | 0 | 800 | 50 | 6.7 | 33 | |

[a] The caproic acid was 22% in this run based on the sodium. [b] The caproic acid was 40% in this run based on the alkyl chloride. [c] Weighed as the hydrate. [d] Only 2% of the sodium went to a Wurtz reaction in this preparation.

The experimental conditions employed in the syntheses of acids from other organic chlorides are tabulated in Table IV. Yields are approximate since the analytical method was perfected for the products of the reaction with amyl chloride only. The results given for methyl, ethyl and propyl

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[4] Norris, "Organic Syntheses," Coll. Vol. I, 1932, p. 137.

TABLE IV

| Chloride | Ml. | Ligroin, ml. | Carbon dioxide, lb. | Sodium, g. | Init. temp., °C. | Yields of organic acids, percentage based on | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Sodium | | Chloride | |
| | | | | | | mono- | di- | mono- | di- |
| *n*-Amyl chloride | 50 | 100 | 120 | 3.5 | 30 | 22 | 39 | 23 | 40 |
| *n*-Butyl chloride | 100 | 150 | 250 | 23 | 90 | 9 | 14 | 10 | 15 |
| *n*-Propyl chloride | 90 | 150 | 260 | 23 | 176 | Tarry products | | | |
| Ethyl chloride | 30[a] | 100 | 220 | 8.3 | 110 | 1 | 4 | 1.3 | 6.5 |
| Methyl chloride | 50[a] | 100 | 200 | 13.3 | 110 | Traces | | | |
| 2-Chloropentane | 120 | 100 | 240 | 23 | 150 | 34 | 13 | 39 | 19 |
| 2-Chloro-3-methylbutane | 120 | 100 | 220 | 2.3 | 30 | 0.5 | 6 | 1 | 10 |
| *n*-Hexyl chloride | 100 | 100 | 340 | 10.8 | 76 | 18 | 9 | 30 | 15 |
| Cetyl chloride | 60[a] | 50 | 200 | 6.3 | 50 | 4 | 14 | 9 | 30 |
| Benzyl chloride[b] | 50 | 100 | 120 | 10 | 200 | 1 | 1 | | |

[a] Quantity in grams. [b] The autoclave should be copper plated when benzyl chloride is used. When the experiment was carried out in the presence of iron a side reaction took place which caused the pressure to rise above the reading of the gage.

chlorides in particular may be lower than the actual amount present.

## Conclusions

Further studies have been made of the preparation of organic acids by interaction of organic chlorides, sodium and carbon dioxide.

In the case of primary and secondary alkyl chlorides in ligroin as a solvent there was obtained the expected monocarboxylic acids, together with larger amounts of substituted malonic acids. Oxalic and carbonic acids were also present. When the reaction was carried out in benzene as a solvent, iso- and terephthalic acids could be isolated from among the products.

A study of conditions with one chloride showed that a yield of 51% of butylmalonic acid, based on the amyl chloride consumed, could be had. This yield is high enough for the method to be considered as a one-step synthesis in this series.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

# The Hydrolysis of Beta-Hydroxyanthraquinone-beta-*d*-glucoside[1]

BY JOHN H. GARDNER AND W. H. DEMAREE

In connection with our study of the ease of hydrolysis of glycosides derived from hydroxyanthraquinones, we have prepared $\beta$-hydroxyanthraquinone-$\beta$-*d*-glucoside and studied its hydrolysis under conditions similar to those used in a similar study of $\alpha$-hydroxyanthraquinone-$\beta$-*d*-glucoside and $\beta$-*d*-arabinoside.[2] The data obtained may be of diagnostic value in determining the structure of naturally occurring glycosides of hydroxyanthraquinones.

$\beta$-Hydroxyanthraquinonetetraacetyl-$\beta$-*d*-glucoside was prepared by the method of Müller.[3] This was hydrolyzed to the glucoside by the method of Robertson.[4] Hydrolyses were carried out with 0.050 *N* hydrochloric acid, 0.050 *N* potassium hydroxide and approximately 10% borax solutions as was described for the experiments with $\alpha$-hydroxyanthraquinone derivatives.[2] Since in all cases, the glycosides were insoluble in the reaction medium, it is impossible to compare reaction velocity constants. However, since the samples of all compounds were ground to the same degree of fineness and were treated under identical conditions, the time required for hydrolysis gives some indication of the relative stability.

The results of this investigation are shown graphically in Fig. 1. In addition to the experiments on hydrolysis with acid, alkali and borax, a study was made of the rate of hydrolysis with emulsion. These measurements were made at 37° and so are not comparable with the others, which were made at 100°. They do, however, justify the designation of the glucoside as a $\beta$

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(1) Anthracene Series XI; No. X, THIS JOURNAL, **58**, 597 (1936).

(2) Gardner, McDonnell and Wiegand, *ibid.*, **57**, 1074 (1935).

(3) Müller, *Ber.*, **62**, 2800 (1929).

(4) Robertson, *J. Chem. Soc.*, 1137 (1930).